NEW METHODS FOR SYNTHESES OF ALDEHYDES FROM NATURALLY OCCURRING AND SYNTHETIC ACIDS

THESIS

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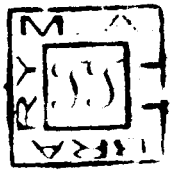

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CERTIFICATE

The work described in this thesis was carried out under my supervision by the candidate **Mr. Md. Omair Zobairi**. It has not been submitted for any other degree, either or this or any other university.

24/8/98

[Professor K.M. Shamsuddin]
(Retd.)
Supervisor

Dedicated
to my
Parents

... and those who remain with me

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INTRODUCTION

INTRODUCTION

Aldehydes are versatile chemical reagents used in organic chemistry and their applications are manifold. They lie in between primary alcohols and carboxylic acids in the oxidation state and because they can be easily reduced or oxidised, it is extremely convenient to proceed on either side of the oxidation chain starting with aldehydes. Addition to the carbonyl group through the cyanohydrin providing the bifunctional α-hydroxy acid, is a reaction which has been used widely. When this reaction is carried out in presence of ammonia α-amino acids are obtained. Aldehydes on mild reduction provide primary alcohols but under different conditions the carbonyl group can be reduced to methylene.

Aldehydes can be conveniently converted into acetylenes, Schiff's bases, amides, amines etc. They can react with aromatic compounds under Friedel and Crafts conditions to give alkylated aromatics. Other useful reactions of aldehydes provide methods of

increasing the chain length, giving rise to differently functionalised compounds through the Perkins, Reformatsky and similar reactions. Examples cited above, though not exhaustive show that aldehydes are indeed versatile reagents.

Apart from their reactivity, several aldehydes are used as a flavouring agents in perfumery and as intermediates in pharmaceutical and dye industries.

This thesis reports two methods for synthesis of aldehydes by the reduction of acid chlorides with formic acid. In one of these the acid chlorides are reduced by formic acid in the basic medium and in the other by catalytic transfer hydrogenation again by using formic acid as the hydrogen donor. In both these methods aldehydes are obtained in extremely good yields. The advantage of these methods also lie in the fact that the reagents and catalysts used are inexpensive, the reaction times very short and the experimental procedure extremely simple.

REDUCTION OF ACID CHLORIDES TO ALDEHYDES

METHODS OF PREPARATION OF ALDEHYDES

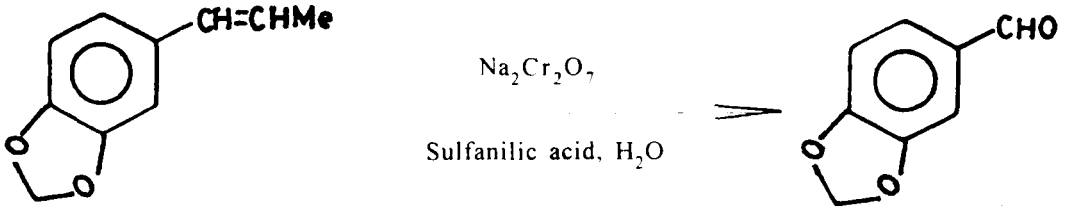
METHODS OF PREPARATION OF ALDEHYDES

This thesis reports two methods for the preparation of aldehydes. It is, therefore, appropriate that the available methods for this purpose be discussed in brief. In the following pages which enumerate methods of preparation of aldehydes the accent is on the methods starting with acid chlorides, as that forms the subject matter of this thesis.

The preparation of aldehyde can be approached in different ways; very broadly either with or without altering the carbon skeleton. This alteration can result in the decrease or increase in the number of carbon atoms originally present in the substrate. Some reactions which represent the former category are the ozonolysis of alkenes[1] (equation 1), oxidation of alkenes with bistriphenylsilylchromate[2] (equation 2), sodium dichromate[3] (equation 3) and ruthenium oxide[4] (equation 4) as exemplified below.

$$C_8H_{17}CH{=}CH(CH_2)_7COOMe \xrightarrow[EtOAc \text{ or } Zn\ HOAc]{O_3,\ MeOH,\ H_2\ Pd\text{-}C} C_8H_{17}CHO \qquad (1)$$

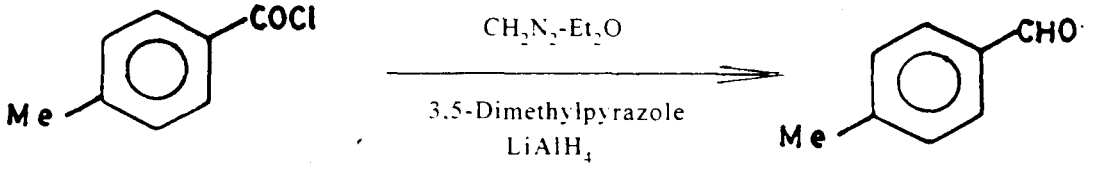
$$PhCH{=}CH_2 \xrightarrow[CCl_4]{\text{Bistriphenylsilylchromate}} PhCHO \qquad (2)$$



(3)

$$C_6H_{13}CH{=}CH_2 \xrightarrow{RuO_4\ CCl_4} C_6H_{13}CHO \qquad (4)$$

The literature similarly bounds with examples of the type in which there is an increase in the number of carbons in the substrate which can be illustrated by the following examples. Treatment of an acid chloride with diazomethane, derivatisation of the homo acid generated followed by reduction yield the homologated aldehydes[5] (equation 5). Alcohols are transformed into allyl ethers which are then rearranged to the aldehyde on treatment with propyllithium[6] (equation 6). Vilsmeier-Haack formylation is a fairly common procedure for preparation of aldehydes[7] (equation 7). The Hoesch condensation is a particularly useful technique in the aromatic series[8] (equation 8).



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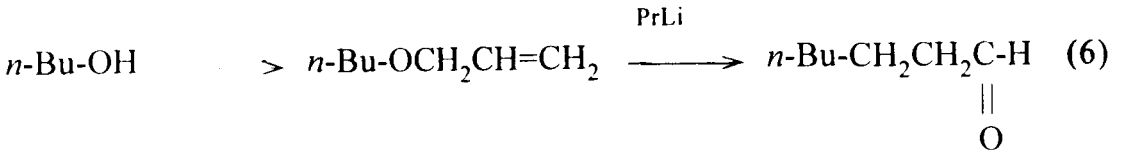

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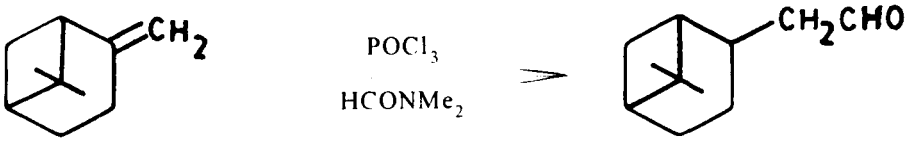

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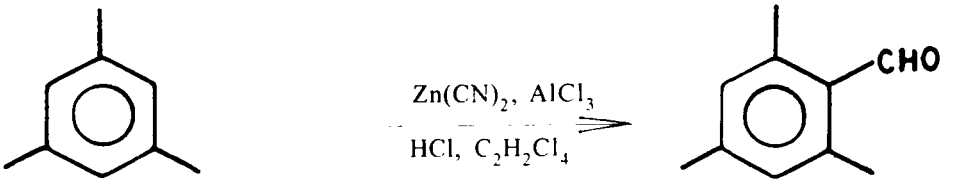


(8)

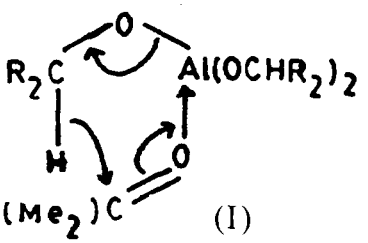
The oxidation state of aldehydes being situated between those of primary alcohols and carboxylic acids, the aldehydes can be approached through the oxidation of primary alcohol or reduction of the acid or its derivatives. In these instances the derived aldehyde invariably have the same carbon skeleton as the starting material. However, it has been observed that though conceptually sound, these methods are procedurally difficult as the aldehyde formed can be easily oxidised or reduced further, depending upon whether they are prepared by oxidation or reduction. The experimental conditions thus have to be designed to stop the oxidation/ reduction reaction at the aldehyde stage. The higher volatility of the aldehydes vis-a-vis the alcohol has, however, made it possible to distil the aldehyde as it is formed from the reaction mixture; especially in case of lower aldehydes.

In the preparation of aldehydes by oxidation of alcohol the more commonly used oxidant is Cr(VI), wherein Cr(VI) is reduced to Cr(III). The Cr(VI) reagents used for this purpose are acid dichromate[9], dipyridinium chromate (Collin's reagent)[10], pyridinium dichromate[11], pyridinium chlorochromate (Corey's reagnet)[12], and chromic acid and H_2SO_4 in water (Jone's reagent)[13]. Where the substrate is acid sensitive CrO_3 in HMPT[14], CrO_3 in pyridine[15] or $Na_2Cr_2O_7$ in water[16] are convenient oxidants. Polymer supported chromium(VI) reagent has also been utilised by adsorbing CrO_3: pyridine (1:2) on celite[17].

Among the manganese based regents activated MnO_2 is an efficient reagent, which is of particular use in the oxidation of allylic alcohols to the corresponding αβ-unsaturated aldehydes[18].

Ceric ammonium nitrate[19], polymer supported silver carbonate (Fetizon's reagent)[20], nitric acid in aqueous glyme[21] and N-methylmorpholine -N-oxide[22] with a ruthenium complex are other reagents used for the oxidation of alcohols.

The Oppenauer oxidation of alcohols to aldehydes is carried out by use of aluminium-t-butoxide in presence of a ketone[23]. This reaction is pictured to take place through a cyclic transition-state (I).



(I)

Catalytic dehydrogenation has also been employed for the conversion of primary alcohols into aldehydes, though these methods are more commonly employed in the industry rather than the laboratory. Catalysts used for this transformation are copper, silver, mixture of these metals, copper chromite[24] or copper oxide[25].

As has been stated above, acids or more conveniently their derivatives can be reduced to aldehydes. House[26] has reported that the acid chlorides are the most easily reducible of these derivatives and consequently the reduction of acid chlorides has been the most investigated reaction in this respect.

First of these investigations[27] has developed into a general method for the preparation of aldehydes, known as the Rosenmund reduction. It essentially consists of catalytic hydrogenation of the acid chloride wherein the carbon-chlorine bond in the acid chloride undergoes hydrogenolysis. (equation 9)

$$\underset{\underset{\underset{O}{\|}}{}}{\text{R-C-Cl}} + H_2 \xrightarrow{\text{Catalyst}} \underset{\underset{\underset{O}{\|}}{}}{\text{R-C-H}} + HCl \qquad (9)$$

The difficulty encountered in this reaction as already mentioned is the over-reduction of the aldehyde generated to the corresponding alcohol in view of the fact that the aldehydes are themselves very easily reducible[26]. The reaction thus has to be carefully controlled in order to maximise the yield of the aldehyde.

The parameters which can be manipulated to direct the reaction in the desired direction are (a) the catalyst (b) the solvent and (c) the temperature of the reaction.

The catalyst that is used more commonly is palladium on barium sulphate[28]. As the use of this or other catalyst can invariably cause further reduction of the aldehyde, this difficulty has been circumvented by the use of substances known as catalyst poisons or regulators. Substances like mercury, divalent sulphur or amines are the more commonly used poisons. They serve to reduce the activity of the catalyst by reducing the extent of bonding between the catalyst and the substance to be reduced. The most commonly used poison is quinoline sulphur[29] which is obtained by heating a mixture of sulphur and quinoline under reflux[30]. Other regulators which have found application are thioquinanthrene[29,31], thio-urea other sulphur compounds[29], tetramethylurea[32], pyridine and copper[33], thiophene or thiourea[32,34], dimethylaniline[35], ethyldiisopropylamine[36], sodium acetate[37], and 2,6-dimethylpyridine[38].

Though palladium on barium sulphate has been widely used, other catalysts found to serve the same purpose are palladium supported on kieselguhr[29,39], charcoal[39,40], or calcium carbonate[41]. Palladium also has been frequently substituted by other metals viz: osmium[40], platinum[33,42,43] and nickel[27,42,43,44,45].

The solvents used should be inert under the reaction conditions or in other words should be inert to hydrogenation. Further it should also be possible to maintain the desired temperature by heating or refluxing. Accordingly aromatic hydrocarbon are the more common solvents; those of common applicability being benzene, toluene or xylene.

In a study of the reduction of higher fatty acid chlorides[46] it was observed that amines when used as acid scavengers were prone to react with acid chlorides and contaminate the products.N,N-Dimethylacetamide was found to be more effective in neutralising the evolved HCl.

The reduction is facile in some cases at the ambient temperature. Elevated temperatures employed for reduction of aliphatic, hydroaromatic and aliphatic aromatic aldehydes vary from 50°C to 200°C. In the preparation of aromatic aldehydes, apart from room temperature in some instances, the temperature used vary from 100°C to 185°C. In the case of heterocyclic aldehydes also a similar situation prevails. These temperatures can be easily maintained by using a suitable solvent and conducting the reaction at the reflux temperature.

A modification of the Rosenmund reduction involves the use of the homogenous hydrogenation catalyst, dihalobis-(triphenyl

phosphine) palladium(II)[47]. It has however been observed that this catalyst was effective only in the reduction of aromatic acid chlorides to aldehydes and in the case of aliphatic substrates no significant quantity of the aldehydes could be obtained.

Procedurally the Rosenmund reaction is carried out by bubbling hydrogen through the hot solution of the acid chloride in a suitable solvent in which the catalyst treated with the regulator is suspended. On the average, yields obtained in this reaction vary from 50-80%. More common side reactions in this process are the over-reduction of aldehyde to alcohol or hydrocarbon and the formation of esters and anhydrides. Occasionally ethers are also observed to be formed. Use of gaseous hydrogen and the attendant hazard is however a drawback in this method.

Another method employed for the conversion of acid chlorides to aldehydes involves hydride transfer from a complex metal hydride. Such hydrides are common reducing agents in organic chemistry, the more commonly used reagents being $LiAlH_4$ and $NaBH_4$. $LiAlH_4$ and $NaBH_4$ being powerful reducing agents the activity of reducing agents have to be reduced considerably in order to prevent further reduction of the generated aldehydes. Such more selective reagents are prepared by modifying these reagents. One such reagent, Lithium tri-t-butoxyaluminium hydride is obtaind by treatment of $LiAlH_4$ with stoichiometric amount of tertiary butyl alcohol[48] (Equation 10)

$$LiAlH_4 + 3t\text{-}C_4H_9\text{-}OH \rightarrow (t\text{-}C_4H_9O)_3LiAlH + 3H_2 \qquad (10)$$

Reduction of acid chlorides to aldehydes can be effected by this reagent[49]. This reduction can be carried out either in tetrahydrofuran or diglyme solutions, the preferred temperature being 0°C. Aldehydes have been obtained by the use of this reagent in yields varying from 36 - 85%.

Sodium tri-t-butoxyaluminium hydride[50] has also been investigated as an alternative to $LiAl(t\text{-}C_4H_9O)_3H$[51]. It is prepared in an analogous manner and is soluble in diglyme solution, but only sparingly soluble in tetrahydrofuran. The reduction is hence carried out by treating the solution of the acid chloride in tetrahydrofuran with a solution of the reagent in diglyme. The reduction however, is carried out at the relatively low temperature of -78°C. Moisture, of course, in case of both reagents has to be rigorously excluded. Reduction by sodium alkoxyaluminium hydride is reported to give aldehydes in almost quantitative yields (92-100%). The reaction time required for the conversion of acid chlorides to aldehydes using Lithium tri-t-butoxyaluminium hydride is 2-3 hours whereas for sodium tri-t-butoxyaluminium hydride is 3-4 hours.

Another reagent which serves the same purpose is tributyltin hydride, Bu_3SnH[52,53]. It has been reported that when the reaction is

conducted in the absence of a solvent, the main product was the ester along with varying amounts of aldehydes. However, when the reaction was conducted in solution the main product was the aldehyde. When the alkyl group in the tin hydride is changed the composition of the products also underwent a change and it was observed that the tributyltin hydride was the hydride of choice to convert acid chlorides into aldehydes. The reaction has been modified by adding palladium-catalyst to the reaction mixture[54,55]. The catalysts used were tetrakis-(triphenyl phosphine) palladium (O), various palladium(II)-complexes or $PdCl_2$ in the presence of triphenyl phosphine. Along with this catalyst tributyltin hydride specifically gave the aldehyde in good yields. Other reducible groups if present are not affected. In the absence of catalyst the acid chloride was reduced to aldehydes according to the equation given below (equation 11). In the presence of catalyst, the reaction was found to be more rapid and selective (equation 12).

$$3RCOX + 3R'_3SnH \rightarrow RCHO + RCO_2CH_2R + 3R'_3SnX \quad (11)$$

$$RCOCl + Bu_3SnH \xrightarrow[RT]{Pd(PPh_3)_4} RCHO + Bu_3SnCl \quad (12)$$

The reaction is extremely rapid and the aldehydes are obtained at room temperature by addition of tributyltin hydride to a mixture of acid chloride and palladium catalyst in a solvent. The solvents

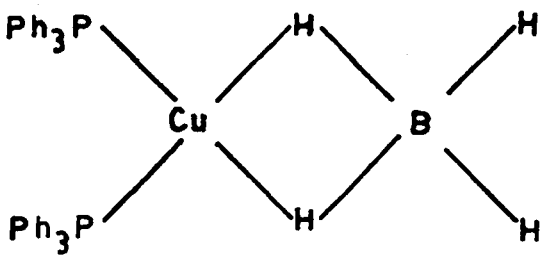
which can be used are benzene, toluene, ether or tetrahydrofuran. A variety of aldehydes have been prepared in yields varying from 70 to 95%. Surprisingly, tetrakis(triphenyl phosphine) palladium (O) catalyses reduction of αβ-unsaturated carbonyl compounds to the corresponding saturated compound whereas in presence of tributyltin hydride the reduction of αβ-unsaturated acid chlorides yielded αβ-unsaturated aldehydes. Reduction of acid chlorides by tributyltin hydride has been postulated to take place through a radical process.

In a closely related method[56] tributylgermanium hydride has been used to reduce acid chloride to aldehyde in the presence of tetrakis-(triphenyl phosphine) palladium(O) in hexamethyl-phosphoramide at 80-100°C. 80-93% yields of the aldehyde has been reported. Nitro and αβ-unsaturated aldehydes are obtained without alteration of these functions.

Sodium borohydride, a versatile reducing agent, though less powerful than lithium aluminium hydride, is commonly used to reduce carbonyl groups to the corresponding carbinols. However when the reduction of acid chloride was conducted in acetonitrile in the presence of certain metallic ions like Li^{+}, Mg^{2-}, Al^{3-} etc. along with N,N-dimethylformamide aldehydes were obtained albeit in relatively low yields of 24-50%[57,58]. In a further investigation of this reaction[59], it was observed that when the reaction was conducted in a mixture of dimethylformamide and tetrahydrofuran yield of the aldehydes were

substantially increased, even in the absence of metal salt. However, during quenching the reaction over-reduction of the aldehyde took place. This could be substantially reduced by quenching the mixture with propionic acid, dilute hydrochloric acid and ethyl-vinyl ether. This reaction requires the low temperatuer of -70°C. Aliphatic and aromatic aldehydes in this instance have been obtained in yield of 80-95%. The aldehydes appeared together with some alcohol in ratios ranging from 6:1 to 19:1. It was also observed that sodium borohydride along with cadmium chloride reduced acid chlorides to aldehydes in fair yield ranging from 50-90%. The reaction was conducted in solvents like dimethylformamide, dimethylacetamide or hexamethyl phosphoramine. However dimethylformamide had to be an essential component[58]. In this reaction also a relatively low temperature of -10°C was required. Sodium borohydride in presence of pyridine and dimethylformamide at 0°C has also been used for this conversion[60].

As stated earlier acid chlorides are reduced to alcohols on treatment with sodium borohyride. Different sets of workers[61,62,63,64] have reduced the activity of borohydride by complexing coppertetra hydroborate with phosphine or phosphite ligands. This complex has been described to have the following structure (II). In one of the procedures reported[61] aldehydes were obtained in good yields varying from 67-100% yields. The reaction was conducted at room



(II)

temperature for a period of 30 minutes. Majority of the aldehydes prepared were aromatic. In another procedure[62] the acid chloride in acetone was added to the catalyst and stirred for 80 minutes. In this case also the aldehydes prepared were mainly aromatic with the exception of cinnamaldehyde and nonanal. Yields ranging from 63-100% were obtained. Sorrell et al[64] also conducted reaction at 25°C and the time required was reported as 1 hour. Yields obtained were reported to be good to excellent and the reaction has been represented by the following equation (13).

$$(Ph_3P)_2CuBH_4 + RCOCl \xrightarrow[\text{acetone, } 25^\circ C]{2Ph_3P} (Ph_3P)_3CuCl + RCHO + Ph_3PBH_3 \quad \ldots\ldots (13)$$

It was reported in 1950[65], that aroyl chlorides on treatment with triethylsilane in refluxing ether or with triethylsilane in presence of aluminium chloride gave the corresponding aldehydes in 30-50%

yields. However, it was later reported[66] that temperature required is much more than what is obtained in refluxing ether. Organosilane hydride in presence of palladium catalyst has been reported to cleave carbon-halogen bond in halocarbons[67]. The same group extended this work to the reduction of acid chlorides to aldehydes[68]. They also observed that the incorporation of palladium catalyst (palladium on charcoal) alters the course of the reaction and reaction of acid chloride with triethylsilane gave aldehydes in yields ranging from 28-75%. The reaction was carried out at room temperature. However, sterically hindered acid chlorides gave very poor yields. Later it was observed that the platinum complex *cis*-$[PtCl_2(PPh_3)_2]$ also catalyses the reduction of acid chlorides to aldehydes[69]. The reaction must be carried out at 120°C and yield of the aldehydes obtained were in the range of 2-68%: not very appreciable. It was also observed that in the presence of rhodium catalyst; *trans*-$[RhCl(CO)(PEtPh_2)_2]$ formation of ketone was found to dominate. The overall reaction in this reduction process has been represented as below (equation 14).

$$R_3SiH + RCOCl \longrightarrow R_3SiCl + RCHO \qquad (14)$$

More recently[70] ligands obtained from diacetylmethane on reaction with certain metals together with triethylsilane were reported to catalyse the reduction of some acid chlorides to aldehydes in yields of 13-89% along with Et_3SiCl, RCO_3SiEt_3, RCO_2CH_2R and

RCOOH. The ligands corresponded to the formula $M[CH(COMe)_2]_n$ (M=Cr, Mn, Fe, Co; n=3; M=Co, Ni, n=2).

Acid chlorides have also been reduced to aldehydes by treatment with $Na_2Fe(CO)_4$[71] in tetrahydrofuran at 0°-60°. Quenching with acetic acid was required to liberate the aldehyde. The reaction has been reported to follow the path described in the following equations (15 and 16)

$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}Cl + Na_2Fe(CO)_4 \longrightarrow Na^+[Fe(CO)_4COR]^- + Na^+Cl^- \quad (15)$$

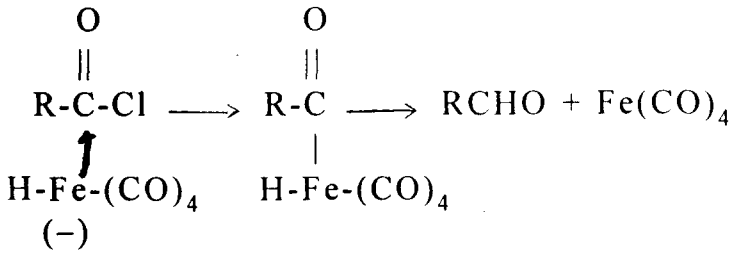
$$Na^+[Fe(CO)_4COR]^- + AcOH \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}H$$

The reaction was conducted in tetrahydrofuran under argon and the overall time requirement was 90 minutes. Aldehydes were obtained in good yields, ranging from 65-95%.

Hydridotetraferratecarbonyl anion has also been used to reduced acid chlorides to aldehydes in good yields in aprotic solvents[72]. The reaction has been represented by the following equation (17).

$$2RCOCl+3NMe_4.HFe(CO)_4 \longrightarrow 2RCHO+2NMe_4Cl+NMe_4HFe(CO) \quad .....(17)$$

and the mechanism by the following steps (equation 18). The reaction



(18)

time varies with the substrate (1-4 hours) and the yields of aldehydes obtained from 80-100%. The efficacy of this reagent is however is in doubt in the preparation of aldehydes from aromatic acid chlorides carrying nitro group and αβ-unsaturated acid chlorides.

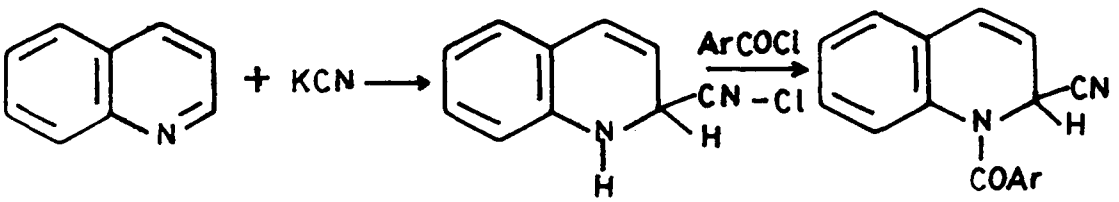
Apart from the methods discussed above for the conversion of acid chlorides to aldehydes, some indirect methods have also been reported to achieve the same results. In the methods discussed above the conversion is secured by hydrogenolysis of the carbon-chlorine bond in the acid chloride by the use of appropriate reagents. In the indirect method the halogen in the acid chloride is displaced by a suitable group, which is then hydrogenolysed. In such cases at least an additional step is involved in the formation of aldehyde.

One of such methods reported involve the formation of a thiolester from the acid chloride which is then subjected to catalytic hydrogenation using Raney-nickel as the catalyst[73]. As expected, the carbon-sulphur bond is cleaved leading to the aldehyde. Steps involved in this reaction can be represented by the following equations (19 and 20).

$$CH_3CH_2\text{-}COCl + C_2H_5SH \xrightarrow[-HCl]{Pyridine} CH_3CH_2\text{-}COSC_2H_5 \quad (19)$$

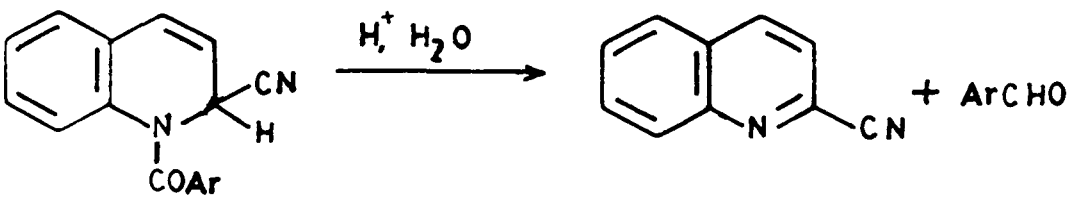
$$CH_3CH_2COSC_2H_5 \xrightarrow[-C_2H_5SH]{H_2\text{-}Ni} CH_3CH_2CHO \quad (20)$$

Hydrolysis of Reissert compounds have also given rise to aldehydes. The Reissert adduct is obtained by the addition of acid chloride to quinoline in aqueous potassium cyanide[74,75] (equation 21).



(21)

The Reissert adduct is then hydrolysed by mineral acids to give the aldehyde (equation 22).



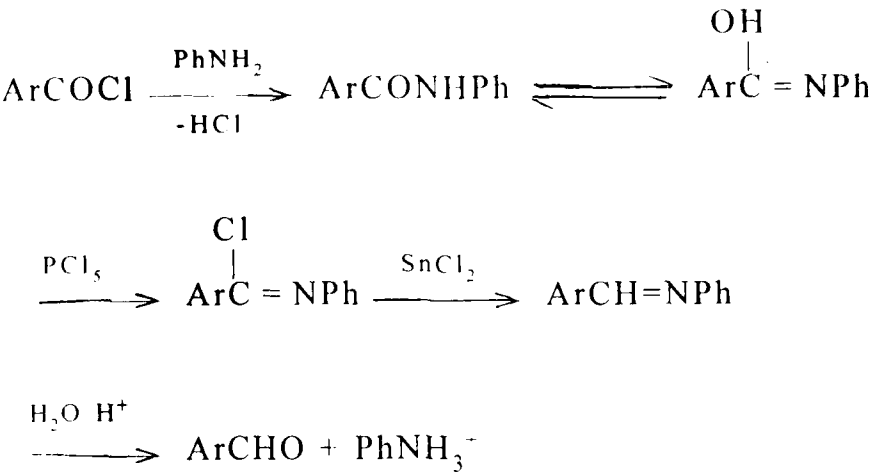
(22)

The Grundmann's procedure is another method used to prepare aldehydes from acid chlorides. Inspite of the fact that this is a circuitous procedure, the overall result has been reported to be satisfactory. This procedure[76] consists of treating the acid chloride with diazomethane to give rise to diazoketones which is subsequently treated with acetic acid at 60-70°C and then boiled. The keto-ester thus generated is reduced by lithium aluminium hydride or aluminium isopropoxide to yield a diol. This diol is then cleaved with lead-tetraacetate or sodium metaperiodate. The overall sequence of reaction involved in this procedure are depicted below (equation 23).

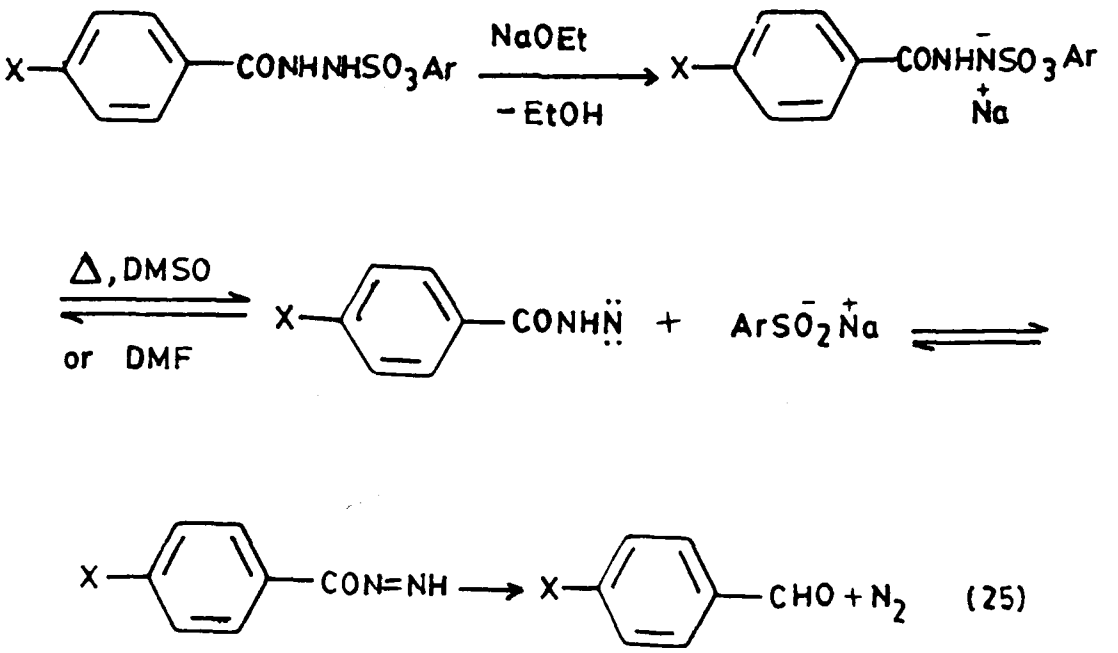
$$\text{R-COCl} \xrightarrow[-\text{HCl}]{\text{CH}_2\text{N}_2} \text{RCOCHN}_2 \xrightarrow[-\text{N}_2]{\text{CH}_3\text{CO}_2\text{H}} \text{RCOCH}_2\text{OCOCH}_3$$

$$\xrightarrow[\text{or Al(OPr}^i\text{)}_3]{\text{LiAlH}_4} \underset{\text{OH OH}}{\text{R-CH-CH}_2} \xrightarrow[\text{or NaIO}_4]{\text{Pb(OAc)}_4} \text{RCHO + HCHO} \qquad (23)$$

In the Sonn-Muller reaction[77] the acid chloride is converted into an anilide or toluide by treatment with the appropriate aryl amine. This amide on treatment with phosphorus pentachloride gives an iminochloride which is reduced with stannous chloride to an imine which is then subjected to acid hydrolysis to yield the aldehyde. Different steps involved in this reaction can be represented as follows (equation 24).

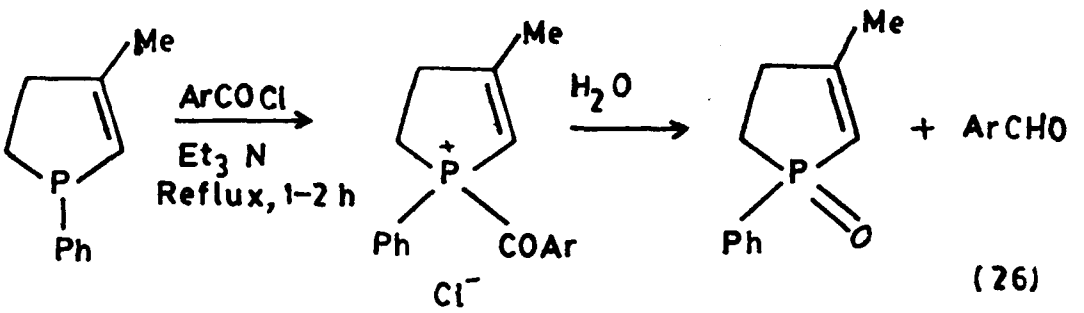


In the closely related McFadyen-Steven method[77], the amide prepared is acyl-sulphonylhydrazide which is obtained either from acid chlorides or esters. Decomposition of the amide has been reported to follow the mechanism[78] depicted below (equation 25).



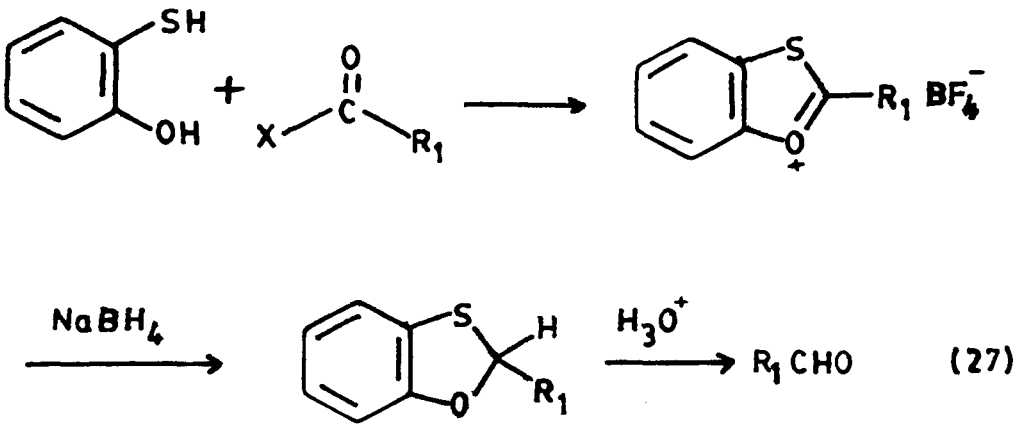
Another method[79] involves the treatment of 3-methyl-1-phenyl-2-phospholene with an acid chloride in presence of triethylamine to

give an acyl-phospholinium salt. This salt on aqueous hydrolysis yields the aldehyde. Only aromatic or heteroaromatic aldehydes have been prepared utilising this method. Yields obtained are in range of 65-89%. Transformations involved in the sequence of reactions can be represented as below (equation 26).

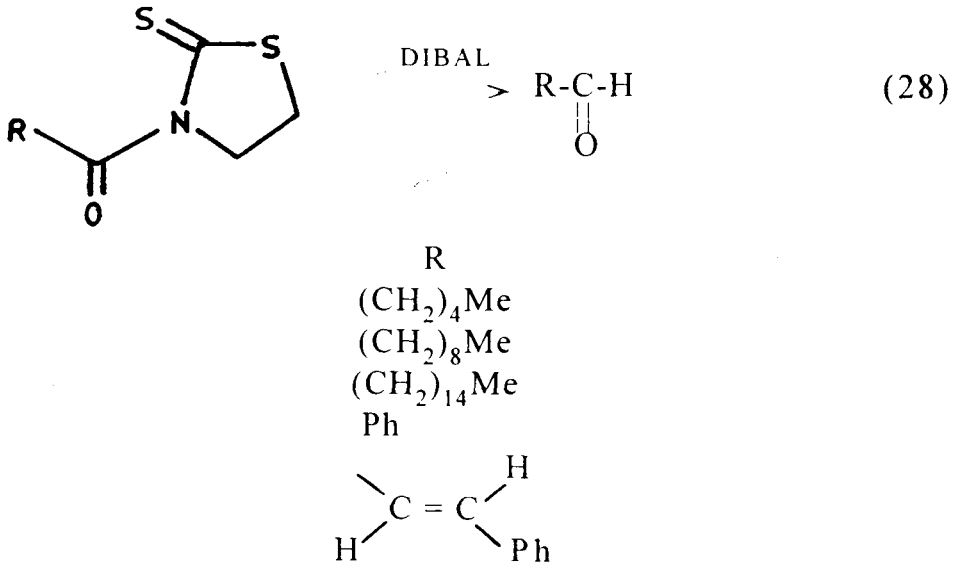


(26)

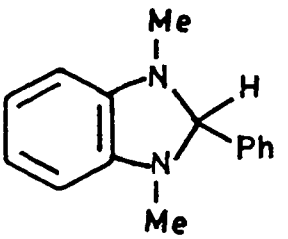
In another indirect method[80] acid chlorides were treated with ortho-mercapto-phenol in tetrafluoroboric acid-ether or borontrifluoride-ether complex to give the heterocylic compound, 2-substituted-1,3-benzoxathiolylium tetrafluoroborate. It was then reduced with sodium borohydride in acetonitrile at 0-20°C to give 2-substituted-1,3-benzoxathiols. Acid catalysed hydrolysis of this compound yielded the aldehyde. Yields obtained in this reaction range from 70-90%. Aliphatic, alicyclic and aromatic aldehydes could be prepared by this method. Transformation taking place during this sequence of reactions are as follows (equation 27)..



The chloride has been replaced by another good leaving group in the amide, 3-acyl-thiozolidine-2-thiones[81]. This amide on treatment with DIBAL yields the aldehyde. The reduction was conducted under argon or nitrogen at temperature varying from -20°C to -50°C. Reduction of the amide with sodium borohydride yielded the alcohols instead of aldehydes. The yields of the aldehydes prepared ranged from 54-93% (equation 28).

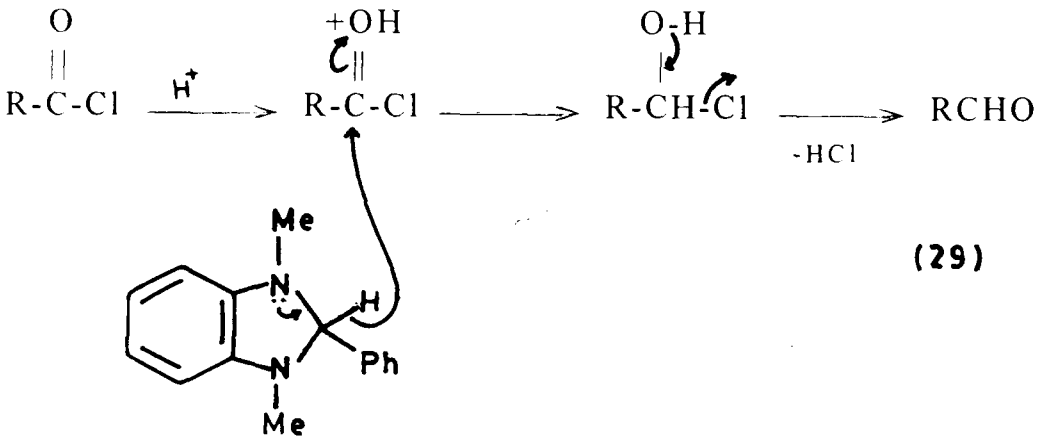


Another approach[82] has been to react acid chloride with 1,3-dimethyl-2-phenyl benzimidazoline (DMBI; III) in acetonitrile in presence of acetic acid all in equimolar quantities. While the reduction was possible even in the absence of acetic acid, it was observed that the presence of equimolar quantity of acetic acid gave better yields (60-90%). The mechanism of the reaction has been explained on the basis of the transfer of hydride ion from DMBI to the carbonyl group



(III)

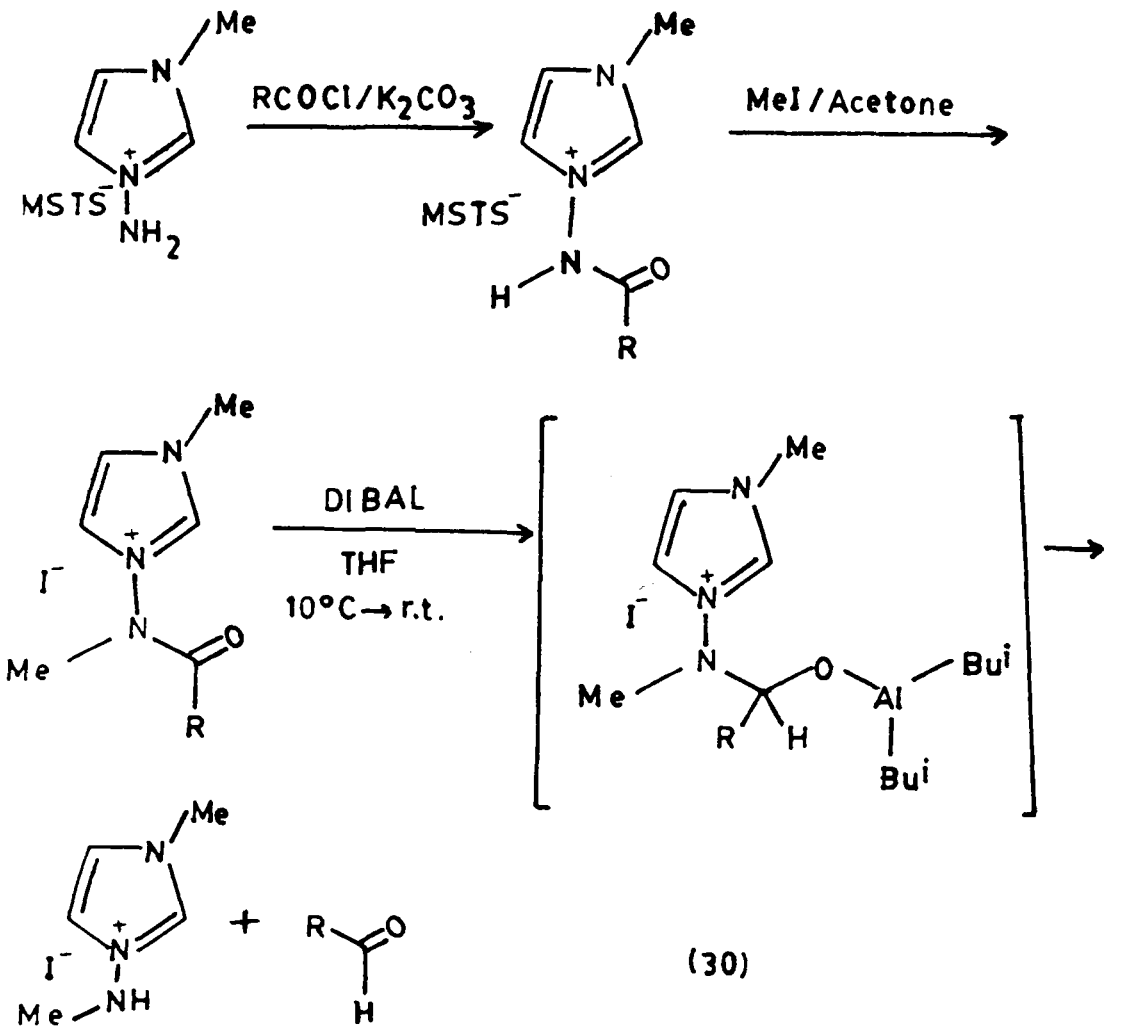
which is electrophilically catalysed by protonation as explained in the sequence of reactions given below (equation 29).



(29)

In a more recent method[83] reported, aldehydes are prepared from acid chlorides via 1-(acylmethylamino)-3-methylimidozolium

ylide, a good leaving group, but treatment with lithiumaluminium hydride, sodium borohydride or lithiumtriethoxy aluminium hydride resulted in the cleavage of the nitrogen-nitrogen bond. However, treatment with diisobutylaluminium hydride in tetrahydrofuran for 30 minutes at temperatures varying from -10°C to room temperature gave good yields of aldehydes. Aliphatic, aromatic and αβ-unsaturated aldehydes were obtained in yields ranging from 69-83%. However the reaction is longwinded and depending upon the substrate low temperatures are also required. Steps involved in this procedure are detailed below (equation 30).



(30)

In another method[84] chlorine of the acid chloride has been replaced by trimethyl phosphonium ion which is formed in situ from an acid chloride and tributyl phosphine in acetonitrile. When this salt is reduced with zinc, copper couple or zinc in methyl sulphonic acid at 0°C in nitrogen atmosphere and then worked up with aqueous 10% hydrochloric acid, followed by 10% potassium carbonate aldehydes were obtained. Yields ranging from 40% to quantitative have been reported. The reaction sequence has been reported as below (equation 31).

$$RCOCl + Bu_3P \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}P^{-}Bu_3 \xrightarrow{Zn\text{-}Cu \text{ or } Zn} \underset{-Bu_3P}{\overset{OH}{\underset{|}{R\text{-}C\text{-}}}P^{+}Bu_3} \longrightarrow RCHO \qquad (31)$$

Methods of preparation of aldehydes are much more than what have been discussed above, but in this instance the main accent of the discussion is confined to the preparation of aldehydes from acid chlorides, as this happens to be the subject matter of this thesis.

FORMIC ACID AS A REDUCING AGENT

FORMIC ACID AS A REDUCING AGENT

In the work being reported the acid chlorides have been reduced to aldehydes by using formic acid as the reductant. It is therefore appropriate to discuss the reducing character of formic acid, which follows.

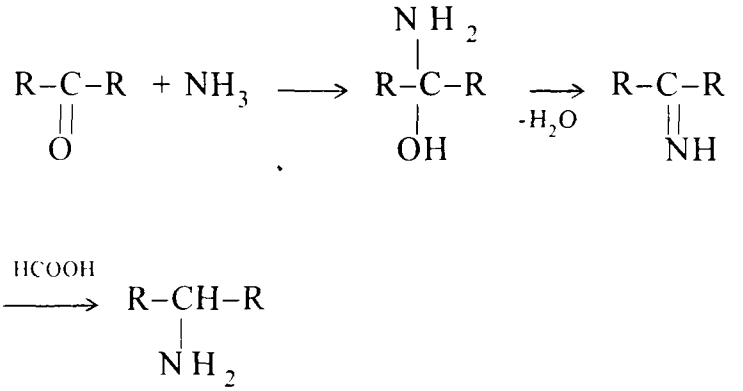
Formic acid differs from other carboxylic acids in that it is endowed with the dual characteristics of an aldehyde and an acid. The reducing character of formic acid can be attributed to the former of these functions. In the broad sense, formic acid is oxidised to the ultimate oxidation state of CO_2 according to the following equation (32).

$$\begin{array}{l} H-C-O-H \\ \quad\| \\ \quad O \end{array} \longrightarrow H_2 + CO_2 \qquad (32)$$

Formic acid has been observed to decompose according to the above known scheme in presence of certain metal or their oxides. Thus on heating with a mixture of copper oxide and chromium oxide at 160°-80° a mixture of CO_2 and H_2 are generated[85]. Alternatively in the presence of

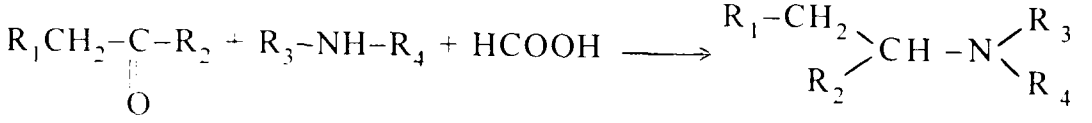
oxygen, platinum, iridium, rubidium or palladium induce a similar decomposition of formic acid at 150°[86]. Several other metals have also been recorded to cause such decomposition of formic acid[87].

Among the substances which have been reported to be reduced by formic acid are imines. The Leuckart reaction in which aldehydes or ketones are treated with ammonia, primary or secondary amines and formic acid at fairly high temperatures yield amines. It is postulated to take place through the intermediacy of imines[88]. A plausible route described is as below[89] (equation 33).



(33)

In the closely related Wallach reaction also formic acid / formate has been identified as the reducing agent.[89] In this process a ketone or an aldehyde reacts with formic acid and formate in presence of a primary or secondary amine to give rise to a higher secondary or tertiary amine respectively, as depicted below (equation 34). In this case also the



..... (34)

reaction has been presumed to proceed through an imine or enamine produced initially by the interaction of the carbonyl compound and the primary or secondary amine respectively. It is then reduced by either formic acid or formate as the case may be.

Another modification of the above set of reactions is the Eschweiler-Clarke reaction[89] in which amines are methylated with formaldehyde and formic acid. In this instance an N-methylene immonium ion generated originally is reduced by the formate ion as depicted below[88] (equation 35). In the above triology, imines formed in-situ are assumed to be reduced by formic acid.

$$R\text{–}NH_2 + \begin{matrix} H \\ \diagdown \\ C = O \\ \diagup \\ H \end{matrix} \longrightarrow R\text{–}\overset{+}{N}H_2\text{–}H_2C\text{–}O^- \rightleftharpoons$$

$$R\text{–}NH\text{–}CH_2\text{–}OH \rightleftharpoons \overset{+}{R}NH = CH_2 \xrightarrow{HCOO^-} RNH\text{–}CH_3 + CO_2 \quad (35)$$

Preformed imines (IV and V) also have been reported to be reduced by formic acid and formate ions[90,91,92,93].

$$ArCH{=}N\text{–}CH_2\text{-}CH_2\text{–}N{=}CH_2 \qquad ArCH{=}N\text{–}CH_2\text{–}CH_2\text{–}N{=}CH\text{–}Ar$$

(IV) (V)

Other substances carrying doubly bonded nitrogens reduced by formic acid are hydrazones and azines to the corresponding hydrazines. In these cases also it has been proposed that the reaction proceeds through the reduction of an imminium ion by hydride transfer from the formate[94,95] (equation 36).

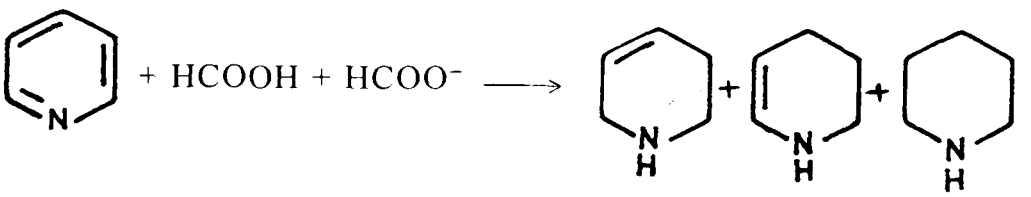
$$>C = N^{+}H + HCOO^{-} \longrightarrow >CH - NH + CO_2 \qquad (36)$$

However one author has differed from this view and has suggested an alternate free radical mechanism[96].

Enamines[97,98,99] are other species which have been reduced using formic acid along with formates. These reactions have again been found to proceed through a hydride transfer to the protonated enamine from the formate[100]. The overall reaction can then be pictured as below on the proof derived from the use of deuterated formic acid as the reductant (equation 37).

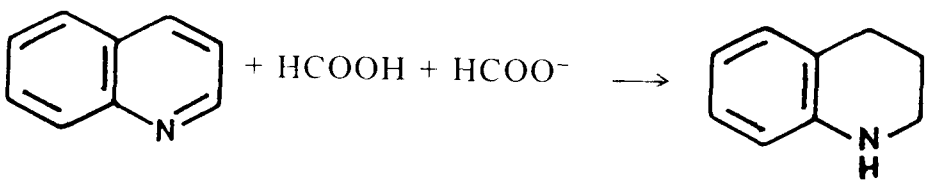
$$HCOOH + HCOO^{-} + HC = C - N \longrightarrow CH - CH \qquad (37)$$

The reduction of pyridine[101] to tetrahydropyridine or piperidine has been explained to proceed through an analogous pathway in view of the latent enamine character of the former (equation 38). Similarly quinolines and

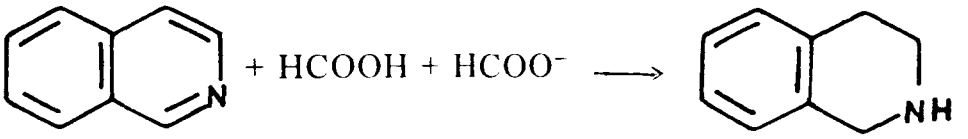


(38)

isoquinolines[102,103] are also reduced by formic acid to the corresponding tetrahydro derivative (equation 39 and 40).

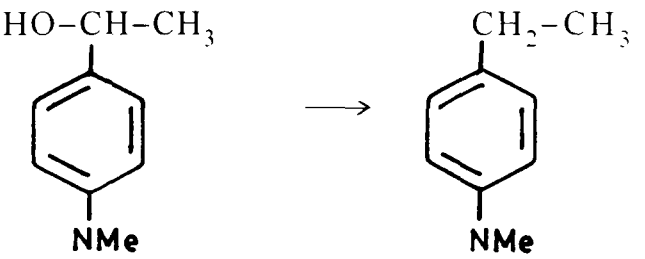


(39)



(40)

Certain alcohols capable of forming fairly stable carbonium ions, subsequent to protonation, have also been reduced, again by a mixture of formic acid and formates. Among such examples cited are the substituted benzylalcohol, α (p-dimethylaminophenyl)-ethanol[91] (equation 41) and triaryl carbinols[104,105] (equation 42) which are reduced to the corresponding hydrocarbons. Though in the former the yield reported is only 6% in the latter it is quantitative. In these instances too, the reactions have been



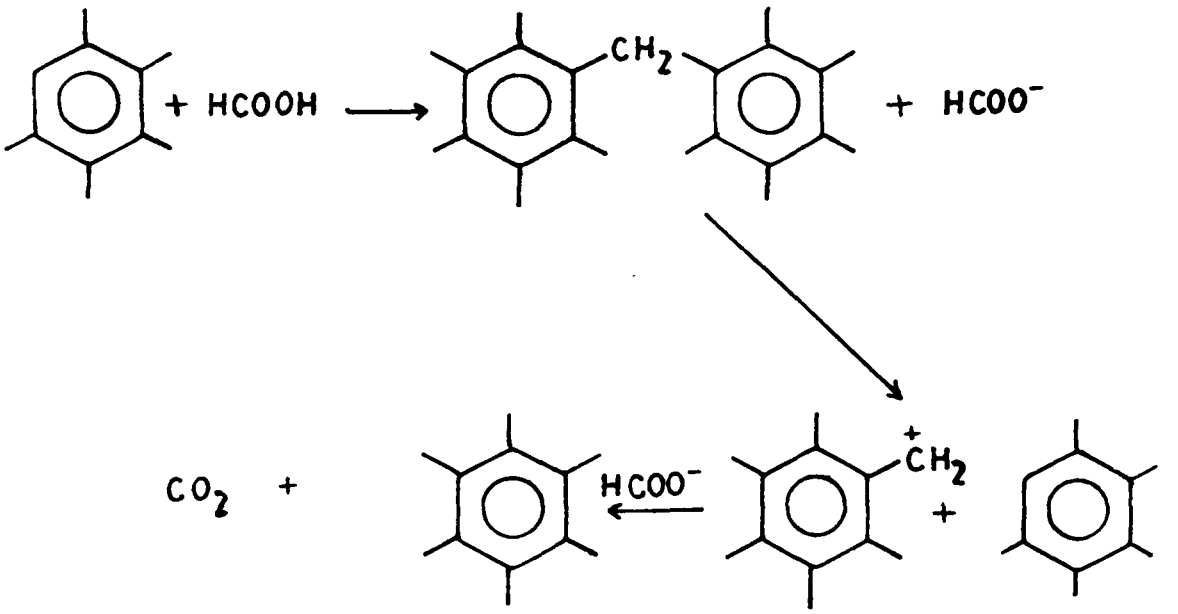
(41)

$$Ar_3C\text{–}OH \longrightarrow Ar_3CH \qquad (42)$$

found to proceed through initial protonation followed by hydride transfer from formate ions. Triaryl methylethylethers and triaryl carbinyl chlorides have also been similarly reduced.[106] Triaryl silanols[107] have been similarly reduced by formic acid, but to arenes (equation 43). Highly alkylated benzenes[108] on treatment with formaldehyde in formic acid,

$$(\phi)_3 - Si - OH \longrightarrow \phi - H \qquad (43)$$

through a series of transformations have been found to yield benzenes which are further alkylated as detailed below (equation 44).



(44)

The above discussion suggests that formic acid is a reducing agent though mild and probably it is because of this characteristic that enough attention has not been paid to the use of formic acid as a reducing agent. The following chapters describe how this potential has been exploited for the preparation of aldehydes from acid chlorides.

CURRENT WORK

CURRENT WORK :

Synthesis of aldehydes by reduction of acid chlorides with formic acid

The previous two chapters have provided a brief survey of the preparation of aldehydes from acid chlorides and the use of formic acid as a reducing agent. The following exercises were went into to examine the feasibility of reducing acid chlorides to aldehydes through a process of hydrogenolysis by using formic acid as a reducing agent.

The purpose of this investigation was to seek alternate ways of reducing acid chlorides to aldehydes. House[26] has listed acid chloride as very easily reducible, the product obtained being aldehyde (Table - I). Discussing details reflecting the selectivity of various reducing agents, $LiAlH_4$ has been reported to reduce acid chlorides to alcohol[109] (Table - II).

TABLE - I

Approximate order of reactivity of functional group in catalytic hydrogenation

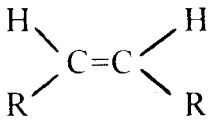
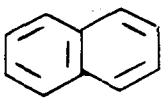
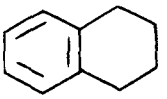
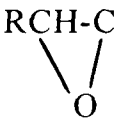
Functional group	Reduction product(s)	Comments
R-CO-Cl	R-CHO	Most easily reduced
$R-NO_2$	$R-NH_2$	
R-C≡C-R		
R-CHO	$R-CH_2OH$	With Pt catalyst, reduction is accelerated by ferrous ion
R-CH=CH-R	$R-CH_2-CH_2-R$	Ease of reduction is decreased by the presence of additional substituents
R-CO-R	R-CHOH-R	
$C_6H_5CH_2OR$	$C_6H_5CH_3+ROH$	
R-C≡N	$R-CH_2NH_2$	
		Also partial reduction of other polycyclic aromatic systems
R-CO-O-R'	R-CH$_2$OH + R'-OH	Pt and Pd catalyst fails to effect these reductions.
		Least easily reduced
$R-CO_2Na$		Inert

TABLE - II

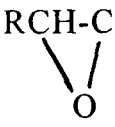
The ease of reduction of various functional groups with $LiAlH_4$ in ether

Substrate	Product	Comment
RCHO	RCH_2OH	Easiest
RCOR	RCHOHR	
RCOCl	RCH_2OH	
Lactone	Diol	
	RCH_2CHOHR	
RCOOR'	$RCH_2OH + R'OH$	
RCOOH	RCH_2OH	
$RCOO^-$	RCH_2OH	
$RCONR'_2$	$RCH_2NR'_2$	
RNO_2	RNH_2	
$ArNO_2$	ArN=NAr	Most difficult
RCH=CHR		Inert

However, they have been found to be inert towards boranes[110] (Table - III).

TABLE - III

The ease of reduction of various functional groups with borane

Substrate	Product	Comment
RCOOH	RCH_2OH	Easiest
RCH=CHR	$(RCH_2CHR)_3B$	
RCOR	RCHOHR	
RCN	RCH_2NH_2	
	RCH_2CHOHR	
RCOOR'	RCH_2OH + R'OH	Most difficult
RCOCl		Inert

In a survey of reducibility of different functionalities by various reducing agents, acid chlorides have been listed to be reduced by all but 2 of the 14 reagents listed which includes catalytic hydrogenation as well[111] (Table - IV)

As has already been stated acid chlorides are very prone to reduction. They are also very susceptible to nucleophilic attack on the carbonyl carbon because of combined - I effects of the halogen and oxygen atoms bound to the carbon. Further, chloride has also been classified as a good leaving group[112].

TABLE - IV

Reactivity of various functional groups with some metal hydrides and toward catalytic hydrogenation ± indicates the borderline case.

Reactions	$NaBH_4$ in Etoh	$NaBH_4$+LiCl in diglyme	$NaBH_4$+AKl$_3$ in diglyme	BH_3 - THF	Bis-3-methyl-2-butyl-borane (diisoamylborane) in THF	9-BBN	$LiAlH(O\text{-}t\text{-}Bu)_3$ in THF	$LiAlH(OMe)_3$ in THF	$LiAlH_4$ in Ether	AlH_3 in THF	$LiBEt_3H$	$(i\text{-}Bu)_2AlH$ (DIBAL-H)	$NaAlEt_2H_2$	Catalytic hydrogenation
$RCHO \rightarrow RCH_2OH$	+	+	+	+	+	+	+	+	+	+	+	+	+	+
$RCOR \rightarrow RCHOHR$	+	+	+	+	+	+	+	+	+	+	+	+	+	+
$RCOCl \rightarrow RCHO$, RCH_2OH	+[a]	+	+	–	–	+	+	+	+	+	+	+	+	+
Lactone→diol	–	+	+	+	+	+	±	+	+	+	+	+	+	+
Epoxide→alcohol	–	+	+	+	±	±	±	+	+	+	+	+	+	+
$RCOOR' \rightarrow RCH_2OH + R'OH$		+	+	±	–	±	±	+	+	+	+	+	+	+
$RCOOH \rightarrow RCH_2OH$	–	–	+	+	–	±	–	+	+	+	–	+	+	–
$RCHOO^- \rightarrow RCH_2OH$	–	–	–	–	–	–	–	+	+	+	–	+	+	–
$RCONR_2 \rightarrow RCH_2OH$, $RCHO$	–	–	–	+	+	+	–	+	+	+	+	+	+	+
$RC{\equiv}N \rightarrow RCH_2NH_2$	–	–	–	+	–	±	–	+	+	+	±	+	+	+
$RNO_2 \rightarrow RNH_2$, $RN{=}NR$	–	–	–	–	–	–	–	+	+	–	–	+	+	+
$RCH{=}CHR \rightarrow RCH_2CH_2R$	–	–	–	+	+	+	–	–	–	–	+	–	–	+

a = Reacts with solvent, reduced in aprotic solvent

These characteristics have been exploited in the conversion of acid chlorides to esters, amides and anhydrides. A reagent which can provide a hydride ion can therefore react with an acid chloride substituting the chlorine with hydrogen to give an aldehyde. However, the possibility of over-reduction to a primary alcohol does exist and this is the product obtained on treatment of acid chloride with $LiAlH_4$, a strong reducing agent. The preparation of aldehyde therefore requires the use of a mild reducing agent and mild conditions. The reducing characteristic of formic acid is rather mild which probably is the reason that comparatively less extensive use of it has been made as a reducing agent. It has also been rarely listed as a reducing agent, except wherein formic acid has been reported to be a hydride donor[99].

Taking together all the facts stated above the possibility of reducing acid chlorides to aldehydes by formic acid appeared to be a distinct possibility. Matter of fact formic acid has been used to prepare aldehydes by making it react with other acids. In this procedure formic acid and another carboxylic acid is heated over thorium oxide[113]. Also the classical text book reaction of conversion of acids to aldehydes involve the heating together of the calcium salt of the fatty acid with calcium formate. It has also been reported that passing vapours of formic acid and other carboxylic acids over MnO lead to formation of aldehydes. In these methods however concomitant

formation of ketones cannot probably be avoided as suggested in the following equations (45 and 46) .

$$Ca(OOCCH_3)_2 + Ca(OOCH)_2 \xrightarrow{\Delta} CH_3CHO + 2CaCO_3 \quad (45)$$

$$Ca(OOCH_3)_2 \xrightarrow{\Delta} CH_3COCH_3 + CaCO_3 \quad (46)$$

The reduction of acid chloride to aldehyde is problematic in basic condition where formic acid is converted into the corresponding salt. Salts of carboxylic acid readily react with acid chlorides to give the corresponding anhydrides (equation 47).

$$CH_3COCl + HCOONa \longrightarrow CH_3-\underset{\underset{O}{\|}}{C}-O-\underset{\underset{O}{\|}}{C}-H + NaCl \quad (47)$$

Investigations were taken into hand keeping the above stated points in view. In all the preliminary studies the acid chloride used was benzoyl chloride as the formation of aldehydes, if any, can be detected olfactorily. Initially formic acid was added to a solution of the acid chloride in chloroform. A vigorous exothermic reaction ensued though formation of no aldehyde could be detected. The reaction between aqueous solutions of sodium formate and benzoyl chloride was also not successful when examined. Modulation of the reaction conditions, viz: variation of temperature, change in concentration etc. did not alter the result.

It was then decided to apply the Schotten - Baumann conditions to this reaction. This procedure has been used in the conversion of acid halides to esters (equation 48). A base is usually used as an acid scavenger to combine with the halogen acid which is formed. If the base used is aqueous alkali this procedure is called Schotten-Baumann procedure[114]. Treatment of ammonia[115] or amines with acid halides to yield amides is also a closely related reaction. These reactions are highly exothermic in nature and have to be controlled by cooling or dilution or both.

$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}X + R'OH \xrightarrow{OH^-} R\text{-}\overset{\overset{O}{\|}}{C}\text{-}OR' + HX + H_2O \qquad (48)$$

It was then decided to use silver formate instead of formic acid. Paralleling Schotten-Baumann conditions the reaction was conducted in aqueous NaOH. Formic acid was added to cold sodium hydroxide, followed by the required quantity of $AgNO_3$ to cause the precipitation of silver formate. To this chilled suspension of silver formate in sodium hydroxide was then added benzoyl chloride in small lots, with constant shaking. After the addition was complete, formation of benzaldehyde was apparent from its distinct smell. However the difficulty faced in developing this reaction further was instability of silver formate, which during the course of reaction

underwent decomposition, the white precipitate turning to grey and finally black.

It was clear from the above exploratory experiments that conditions had to be suitably modified to make this approach a success.

The following emerged from the experience of the preliminary experiments described above.

(a) It is better that the reaction is carried out in basic medium paralleling the Schotten-Baumann conditions. It was also assumed that the translocation of hydride ion shall be more facile in basic conditions. A parallel case of hydride transfer also takes place during self-oxidation reduction of formaldehyde in the Cannizarro reaction[116] which is conducted in the strongly basic medium of 50% KOH (equation 49). Formic acid when added to the basic solution

$$2ArCHO \xrightarrow{KOH} ArCH_2OH + ArCOO^- \qquad (49)$$

shall be converted into its salt and the cation could exert an electrophilic catalytic effect by pulling the Cl^- away from the carbonyl carbon thereby, also increasing the electrophilicity of the carbonyl carbon. Thus the attack by the hydride ion is facilitated leading to an overall push-pull effect[117].

(b) Secondly, the direct and immediate contact between the salt of formic acid and an acid chloride shall lead to the formation of the

anhydride. Conditions therefore have to be so devised that the contact between the reactants are minimised to reduce the possibility of the nucleophilic attack of the formate on the carbonyl carbon. It was therefore thought prudent to conduct the reaction in a biphasic medium. an organic solvent to dissolve the acid chloride and an aqueous base, paralleling the Schotten-Baumann conditions. Formic acid then could be added to the base. precluding the use of preformed salts. Additionally under these circumstances the absence of free formic acid would avoid any possible complications during the reactions and also make the workup of the reaction mixture considerably convenient by preventing the dissolution of formic acid in the organic layer. Under these conditions the minimal contact between the base and acid chloride shall also reduce the likelihood of hydrolysis of the acid chloride. and also formation of the amide if the base used is ammonium hydroxide. Thereby the reaction shall be, to the maximum extent possible directed towards the formation of aldehydes. minimising if not avoiding side reactions.

Preparation of Benzaldehyde

Taking all the above into consideration the benzoyl chloride was dissolved in chloroform (27% w/v) and covered by a layer of liquour ammonia (25%) in a round bottomed flask. Nitrogen was passed through this liquid to deoxygenate the solution. To this liquid

during stirring, was added formic acid gradually, taking care that the solution remained basic. The quantity of formic acid used was three-times in relation to the acid chloride. The addition was done over a period of 45 minutes and the stirring continued further for a short duration. During the whole course of reaction a thin stream of nitrogen was passed through the reaction mixture. The contents were then transferred into a separating funnel and the chloroform layer separated. The organic layer was then washed with water to remove the residual ammonia. To the chloroform layer obtained was added dry sodium sulphate to remove all traces of water. The chloroform was then recovered to yield a liquid which could be identified as benzaldehyde on the basis of its characteristic smell.

The liquid product when tested with aldehydic reagents gave positive results. Thus, it gave a silver mirror with the Tollens' reagent and a green precipitate with the Benedict's solution. Expectedly, as reported, it tested negative with Fehling's solution.

From the above tests the presence of an aldehydic function in the liquid was apparent. The homogeneity of this liquid was further tested by GLC. The chromatography was carried out using a glass column of carbowax-200 C maintaining the oven temperature at 150°C. Initially a known sample of benzaldehyde (BDH) was run and the retention time was found to be 4 minutes. A similar run of the isolated liquid also gave the retention time of 4 minutes and the

nature of the peak showed no distortion. In order to further confirm the identity of the isolate the chromatogram was run by using a mixture of the product and authentic benzaldehyde. In this case also a single peak appeared with the retention time of 4 minutes.

Further confirmation of the isolate as benzaldehyde was obtained by derivatisation. It formed a 2,4-dinitrophenylhydrazone, m.p. 235-239°C which tallied with the literature value of 237°C[118,199]. It also formed a phenylhydrazone, m.p. 156-158°C comparable to the reported value of 158°C[118,119]. The refractive index of the isolated liquid determined as 1.522 very close to the reported value of 1.5456[118,119].

Examination of the IR spectra of benzoic acid, benzoyl chloride and benzaldehyde further provided proof to the identification of the product as benzaldehyde. In the carbonyl region, the acid absorbed at 1710 cm^{-1}, the chloride at 1780 cm^{-1} and the product at 1705 cm^{-1}. Futher there was no absorption in the hydroxyl region in both the cases of the benzoyl chloride and the isolate.

The final proof of the identity of the product was obtained from its NMR spectra determined in $CDCl_3$. The deshielded aldehydic proton appeared as a singlet at δ9.95 integrating for one proton and the five aromatic protons at 7.75 as a 2H multiplet and at 7.5 as a 3H multiplet, which was in total agreement with the published spectra of benzaldehyde[120] (VI). The yield of benzaldehyde obtained was

C_6H_5-CHO

(VI)

extremely good, being recorded as 79%. Having thus succeeded in the attempt to convert benzoyl chloride into benzaldehyde using formic acid as the reducing agent, it became necessary to identify the conditions to optimise the yield. The variables in this reaction are the identity of the reactants, concentration of the reactants, the pH at which the reaction is conducted, medium of the reaction, the temperature at which the reaction is carried out and the atmosphere in which the reaction is conducted.

Identity of the reactants

Working onward from the preparation of benzaldehyde detailed above, the reaction conditions were varied initially by changing the reactants. The acid chloride being the substrate the reactant which can be subjected to change was the reducing agent. When formic acid is added to ammonium hydroxide the ammonium formate formed should be the actual reductant. The reaction was varied by adding sodium formate to the ammonium hydroxide under conditions which no ammonium hydroxide shall be consumed. Under these conditions also the reaction went very smoothly. Therefore it was concluded that

either of the two following conditions are equally successful viz;

(a) ammonium hydroxide + formic acid

(b) ammonium hydroxide + sodium formate

There was no perceptible difference in yields of the aldehyde in either of the conditions. However in the former instance, addition of ammonia might be necessary to maintain the basic nature of the aqueous medium. Another variation attempted was the use of NaOH (0.3 M) as the base instead of ammonium hydroxide. Comparable results were obtained in this case also.

Concentration of the reactants

The ammonium hydroxide used to start with was of the concentration of 25%. Attempts at dilution of this led to the following difficulties: (a) the bulk of the aqueous phase increased and (b) the tendency to form emulsions was more prevalent, making the work up of this reaction mixture more troublesome. Increasing the concentration of the chloroform solution tended to reduce the yield. The concentration, depending upon the substrate, found most suitable was 20 to 30% (w/v).

pH of the medium

The pH of the aqueous medium was varied from 7-12 and the yield of the product examined. At pH 7, yield of the aldehyde was

insignificant. The pH was modulated by changing the concentration of the ammonia and also by adding NH_4Cl to it. The observations recorded are as follows (Table V; Graph I).

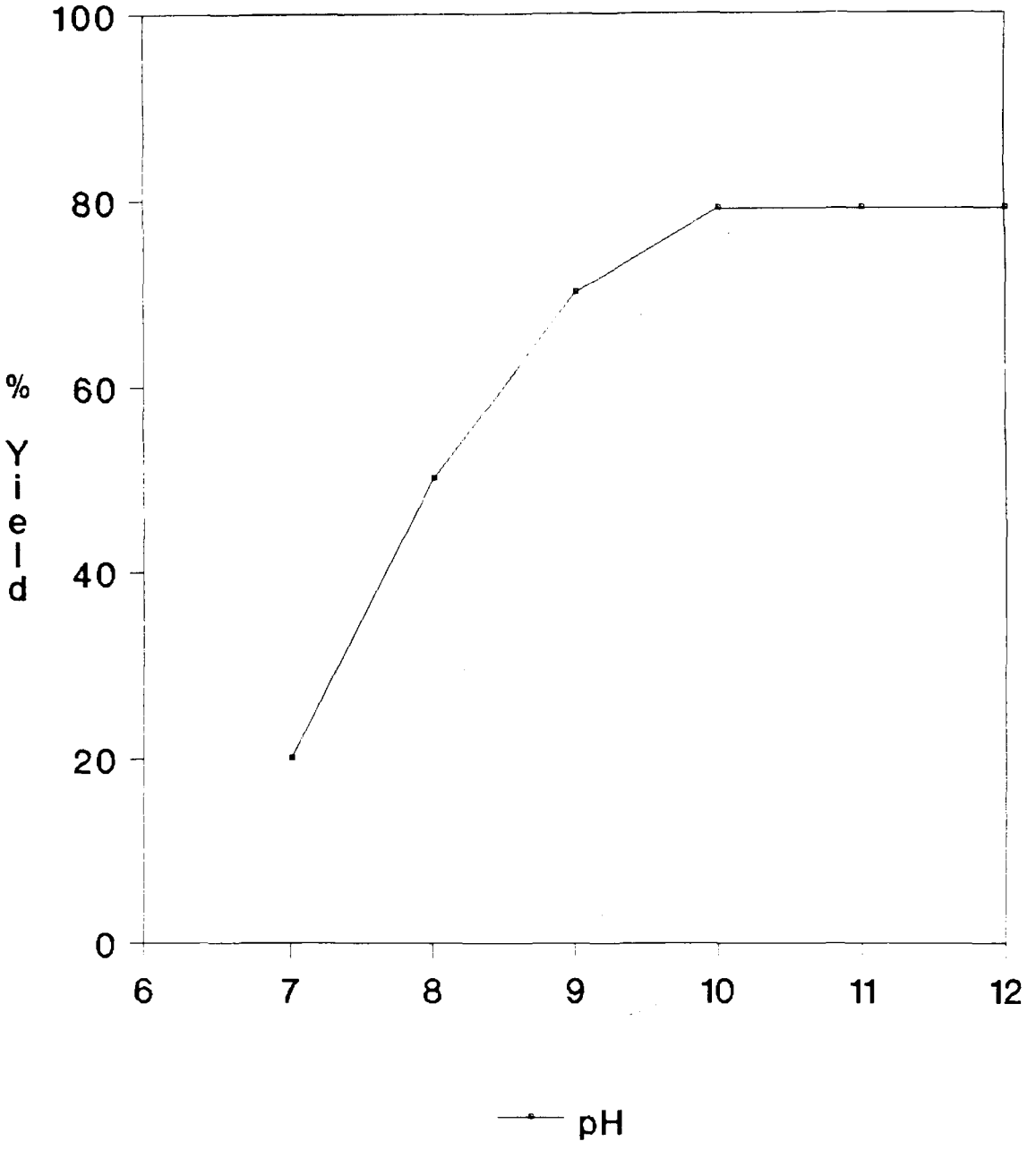
TABLE - V

pH	medium	yield
7	water	~20%
8	NH_3	50%
9	NH_3	70%
10	NH_3	79%
12	NH_3	79%
12	NaOH	79%

It could be concluded from the above that the optimum pH at which the reaction can be conducted obtain the maximum yield is 10.

Medium of the reaction

The reaction being run in biphasic medium there are in essence two mediums, the organic phase and the aqueous phase. The conditions which would determined the suitability of the organic medium are (a) its immiscibility with water, (b) tendency to form emulsion, (c) its volatility on which the ease of work up the reaction mixture depended and (d) the temperature at which the reaction is carried out.



Graph I

Taking the above points into consideration, the solvents studied were ether and chloroform as the reactions were invariably conducted at room temperature. While both were efficacious and there was hardly any choice between the two except that, when ether was used, frequent replenishment was necessary to keep its volume constant. Therefore chloroform in the majority cases was found to be more convenient. In the case of the aldehydes which boil at temperature below the boiling point of chloroform, ether was found to be more appropriate.

In the case of the aqueous medium, it had already been observed that the optimum pH at which the reaction is best conducted is 10. Hence it was decided to use the most easily accessible bases: ammonium hydroxide or sodium hydroxide. In both the mediums the reaction ran with equal facility and preference was accorded to ammonium hydroxide as solution of 25% concentration was easily available, whereas solutions of sodium hydroxide of appropriate concentrations had to be prepared. However had their been side reactions leading to the formation of amides or amines, ammonium hydroxide would have been less suitable. As no such side reactions were found to take place, the aqueous base used was ammonium hydroxide.

Temperature

The reaction ran successfully at the ambient temperature. At higher temperatures the reaction did go faster, but the product was

accompanied by side products. However in certain instances it was found necessary to employ lower temperature to control the reaction as indicated by the rate of evolution of CO_2. The reaction was best run between 15 °C and 25 °C, in the majority of cases towards 25°C.

Propionaldehyde

The compound first prepared being an aromatic aldehyde, it was then decided to examine whether this method would be equally applicable to prepare simple aliphatic aldehydes or not. Logically acetaldehyde should have been the first to have been attempted to prepared. However anticipating the difficulty that would have to be encountered in isolating the aldehyde from the aqueous medium and by evaporating ether or chloroform as the case may be, because of its low boiling point, it was decided to try and prepare propionaldehyde.

Propionoyl chloride was prepared by the treatment of propionic acid with thionyl chloride. The chloride thus prepared was dissolved in ether (20%; w/v) and covered with a layer of ammonium hydroxide and both the layers deoxygenated by passing a stream of nitrogen through them, while the liquid was being stirred. Formic acid was added to the mixture gradually at room temperature. The addition was accompanied by effervescence indicating the evolution of CO_2; which ceased after 40 minutes. The stirring was continued for another five minutes and the reaction mixture worked up by washing the ether

layer, drying it over dry sodium sulphate and evaporating the solvent. The liquid thus obtained absorbed in IR at 1710 cm^{-1} compared to 1720 cm^{-1} by the acid and 1800 cm^{-1} by the chloride. Its aldehydic nature was evident from the positive reactions it gave with Tollens' and Fehling's solution. It also formed a 2,4-dinitrophenylhydrazone m.p. 152-56°C (155°C)[118,119] compared to the literature value given in parenthesis. The homogeneity of the sample was confirmed by GLC on a column of carbowax-200 C maintained at 80°C when only one peak was obtained characteristic of the compound with the retention time of 1.8 minutes. The liquid was thus identified as propionaldehyde (VII) on the basis of its refractive index of 1.376 against the reported value of 1.3636[118,119]. Compared to the acid chloride used, it was obtained in an yield of 79%.

$$CH_3CH_2CHO$$

(VII)

Butyraldehyde

The next preparation attempted was that of butyraldehyde. In this instance, butyryl chloride was obtained by the treatment of butyric acid with thionyl chloride: the standard procedure. The acid chloride was dissolved in chloroform (20%: w/v), ammonium hydroxide (25%) added to it, the solutions deoxygenated by passing

nitrogen through them and three fold formic acid in relation to the quantity of the acid chloride gradually added to this biphase medium with continuous stirring till the evolution of CO_2 ceased i.e. 30 minutes. The stirring was continued for another 5 minutes and the reaction mixture worked up to yield butyraldehyde (VIII) in 90% yield. Butyraldehyde (VIII) gave positive reactions with the Tollens'

$$CH_3CH_2CH_2CHO$$

(VIII)

and Fehling's reagents and was found to be homogeneous on GLC examination with a retention time of 6.12 minutes. The identity was finally confirmed from its observed refractive index of 1.411(1.379)[118.119] and the 2,4-dinitrophenylhydrazone prepared m.p. 118-24 °C which tallied with the value reported in the literature 123°C[118.119].

Phenylacetaldehyde

The next aldehyde to be prepared was phenylacetaldehyde which carries a relatively bulky substituent on the α-carbon. The acid chloride in this case was prepared by reacting phenylacetic acid with thionyl chloride under the catalytic influence of dimethylformamide. The chloride, dissolved in chloroform (33%, w/v) was covered with 25% ammonium hydroxide solution and the total liquid deoxygenated by passing nitrogen through it. The mixture was

stirred while nitrogen was being passed through it continuously and formic acid; thrice the quantity of the acid chloride gradually added to it. During this addition there was a persistent evolution of CO_2 and after CO_2 ceased to evolve. the mixture was further stirred for another 5 minutes, the total period of reaction being 50 minutes. The chloroform layer was isolated, washed with water and dried over anhydrous sodium sulphate. Recovery of chloroform yielded a viscous liquid. This liquid responded to tests with aldehydic reagents. The product when examined by GLC was founed to be homogeneous with a retention time of 3.68 minutes. Identity of the product as phenylacetaldehyde (IX) was established by preparation of 2,4-dinitrophenylhydrazone m.p. 126-28°C, which tallied with the reported

$$C_6H_5-CH_2-CHO$$

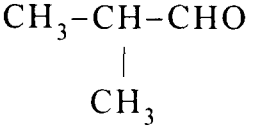
(IX)

m.p. of 126°C[118.119]. The refractive index of this liquid was 1.536 against the reported value of 1.5255[118.119].

Isobutyraldehyde

In the cases discussed above, chlorides derived from aromatic or primary acids were successfully converted into aldehydes. Therefore it was decided to examine the feasibility of converting

secondary acids through their chlorides into aldehydes. The treatment of isobutyric acid with thionyl chloride in the absence of any solvent conveniently yielded the acid chloride. To the solution of acid chloride in chloroform (27%; w/v) was added ammonium hydroxide (25%), the mixture deoxygenated by passing nitrogen and then three fold formic acid gradually added to the mixture with continuous stirring. Compared to the previous preparations in this instance the evolution of CO_2 was much more rapid and the reaction much quicker as evidenced by the lesser time of 25 minutes required for completion of the reaction. The product isolated from the chloroform layer gave positive tests with the aldehydic reagents and also was found to be homogeneous on GLC examination with a retention time of 4.72 minutes. The identity of the product as isobutyraldehyde(X) was

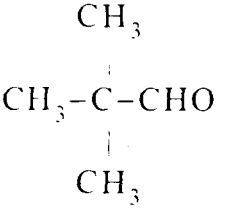


(X)

established by determination of the refractive indcx of 1.401 for it, against the reported value 1.372[118.119]. It also formed a 2,4-dinitrophenylhydrazone m.p. 188-192°C which tallied with the reported value of 187°C[118.119].

Pivalaldehyde

Having observed that both the primary and secondary acid chlorides can be reduced to the corresponding aldehydes, it was but natural to examine whether tertiary acid chlorides also can be reduced to the aldehydes. Accordingly the most easily available pivaloyl chloride was examined from this view. A solution of pivaloyl chloride (E. Merck) in chloroform (27%; w/v) was treated with ammonium hydroxide (25%) and to this deoxygenated mixture was added thrice the quantity of formic acid in relation to pivaloyl chloride gradually, continuing the passage of nitrogen through the liquid. In this case the evolution of CO_2 was particularly fast and the reaction was completed within 20 minutes. Work up of this mixture in the manner described earlier yielded a liquid which tested positive to Tollens', Fehling's and Benedict's reagents. The aldehyde so obtained was identified as pivalaldehyde (XI) on the basis of its refractive index of 1.398 as against the reported value of 1.379[118,119]. Further the melting point of the 2,4-dinitrophenylhydrazone also tallied with the reported value, viz: 207-211°C (209)[118,119].



(XI)

Surprisingly, the tertiary acid chloride was the most easily reducible when compared to the secondary acid chloride which was more easily reducible than the primary.

Monochloroacetaldehyde

It was also necessary to identify the substituents and functionalities which can interfere in this reaction. Hence, it was thought desirable to check whether any halogen present in the substrate shall affect this reaction or not. Hence the chloride of chloroacetic acid was prepaed by treatment of monochloroacetic acid with thionyl chloride. The isolated acid chloride was dissolved in chloroform (27%; w/v), ammonium hydroxide (25%) added to it and the liquid deoxygenated. Three fold formic acid was added to it gradually with stirring continuing the passage of nitrogen. The reaction was completed in 45 mintutes. Work up of the reaction mixture yielded a liquid which was found to be an aldehyde on the basis of its positive reactions towards common aldehydic reagents. GLC examination indicated it to be homogeneous with its peak appearing with the retention time 4.2 minutes. Identity of this aldehyde was established as monochloroacetaldehyde(XII) on the basis of its refractive index 1.435 (1.403)[118.119] and the 2,4-dinitrophenylhydrazone prepared m.p. 108-110°C.

$Cl\text{-}CH_2\text{-}CHO$

(XII)

2-chloropropionaldehyde

Extending this approach of verifying the possible deleterious action of halogen present on the substrate in this reaction, the study was extended to 2-chloropropionic acid. The chloride prepared from this acid was reduced with formic acid using the general method described earlier. Recovery of chloroform gave a liquid found to be an aldehyde on testing with Tollens' and Fehling's reagents. It was also found to be homogeneous on GLC examination with a sharp peak appearing with the retention time of 6.8 minutes. The identity of this aldehyde was established as 2-chloropropionaldehyde(XIII) on the basis of its refractive index 1.441 (1.431)[118,119] and the melting point of its 2,4-dinitrophenylhydrazone 137°C.

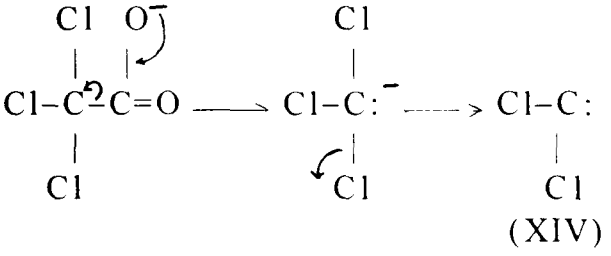
$$CH_3\text{–}\underset{\displaystyle Cl}{\underset{|}{CH}}\text{–}CHO$$

(XIII)

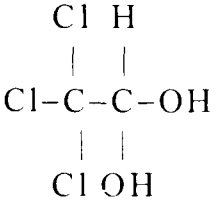
Trichloroacetaldehyde

In continuation with the studies conducted on monochloro substituted acid chlorides it was also thought desirable to examine

whether trichloro acetic acid can provide the aldehyde through its acid chloride or not. In this instance a probable complication could be the formation of dichlorocarbene(XIV) by the interaction of trichloroacetic acid with the base present. The chloride derived from trichloroacetic acid was reduced with formic acid in the manner described above under nitrogen. The reaction was over in 50 minutes as indicated by the ceasage of evolution of CO_2. Evaporation of the chloroform layer gave a solid along with a liquid. The solid melted at 53°C and was identified as chloralhydrate m.p 55°C[118,119] (XV).



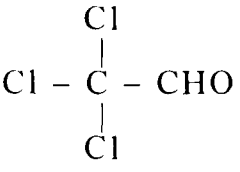
(XIV)



(XV)

The liquid portion was found to be an aldehyde on testing with aldehydic reagents. It was also observed to be homogeneous on GLC examination with retention time of 2.28 minutes. It formed a 2.4-dinitrophenylhydrazone m.p. 130-34°C (131°C) and had a refractive

index 1.449(1.45572)[118,119] leading to its identification as trichloroacetaldehyde (XVI).



(XVI)

It is evident from the preparation of chloroacetaldehyde, 2-chloropropionaldehyde and trichloroacetaldehyde that chlorine if present in the substrate does not interfere in this reaction and this method can be used for the preparation of chlorine containing aldehydes.

Lauraldehyde

Having successfully converted chlorides of primary, secondary, tertiary and chlorine containing acids of relatively lower molecular weight to aldehydes through their chlorides it was decided to examine the feasibility of preparing aldehydes of higher molecular weights starting with the corresponding acids. Lauric acid was first of this series examined. The chloride of lauric acid was prepared by refluxing a mixture of thionyl chloride and lauric acid in benzene for 6 hours. Evaporation of the solvent yielded lauric acid chloride which was dissolved in chloroform (27%; w/v). Ammonium hydroxide (25%) was added to it while the liquid was being flushed with nitrogen.

Formic acid in excess when added to this solution gradually, vigorous evolution of CO_2 took place. Because of the severity of this reaction it was found necessary to cool the reaction mixture. After several exploratory runs ultimately the reaction was conducted at 20°C. Against the average time of 45 minutes required for the reactions conducted earlier, in this case the time required was only 25 minutes. Recovery of the organic layer yielded a semisolid mass which responded positively to aldehydic reagents. The aldehyde was identified as lauraldehyde (XVII) on the basis of the melting point of its 2.4-dinitrophenylhydrazone 104-108°C (106°C)[118,119].

$$CH_3(CH_2)_{10}CHO$$

(XVII)

Palmitaldehyde

The next higher fatty acid examined on these lines was palmitic acid. In this case also the acid chloride was prepared by refluxing the palmitic acid with thionyl chloride in benzene. The acid chloride thus obtained was dissolved in chloroform (27%; w/v), ammonium hydroxide (25%) added to it, and the total liquid deoxygenated by flushing with nitrogen. Formic acid in excess was added to the solution gradually, maintaining the temperature at 20°C. The reaction was completed in 20 minutes. The isolated product which tested positive for aldehyde was identified as palmitaldehyde (XVIII) on

the basis of the formation of its 2,4-dinitrophenylhydrazone m.p. 107-110 °C (105-7 °C)[118,119].

$$CH_3(CH_2)_{14}CHO$$

(XVIII)

Strearaldehyde

The C-18 fatty acid, stearic acid was the next acid which was tested. Treatment of the stearic acid with thionyl chloride in refluxing benzene for 6 hours yielded the acid chloride. To the solution of this acid chloride in chloroform (27%; w/v) was added ammonium hydroxide (25%) followed by gradual addition of excess of formic acid under nitrogen. In this case also evolution of CO_2 was extremely vigorous and hence the reaction had to be conducted at 20°C. The isolated waxy solid tested positive with aldehydic reagents and its m.p. 57-58°C corresponded to the reported melting point of steraraldehyde (XIX) 55°C. It also formed a 2,4-dinitrophenylhydrazone m.p. 124-127°C[118,119].

$$CH_3(CH_2)_{16}CHO$$

(XIX)

Olealdehyde

While saturated fatty acids could be converted into aldehydes through their chlorides, it was of interest to examine whether

unsaturated fatty acids also would respond to this reaction or not. This would also identify the possible interference of isolated double bond in this reaction. Accordingly, the chloride of oleic acid was prepared by refluxing a mixture of oleic acid and thionyl chloride in benzene for 6 hours. The acid chloride thus prepared was dissolved in chloroform (27%; w/v) and treated with formic acid in presence of ammonium hydroxide (25%) at 20°C. The reaction was over in 30 minutes as indicated by the time by which CO_2 ceased to evolve. The isolate reacted positively with the Tollens' and Fehling's reagents. The liquid was identified as olealdehyde (XX), on the basis of its refractive index of 1.456 (1.558) and the derived 2,4-dinitrophenylhydrazone m. p. 67-70°C (67-68°C)[118,119].

$$CH_3(CH_2)_7CH=CH(CH_2)_7CHO$$

(XX)

10- Undecenaldehyde

Another unsaturated acid examined was 10-undecenoic acid. This acid also provided the chloride conveniently by refluxing it with thionyl chloride in benzene for 6 hours. The acid chloride was treated in the same manner by reacting with ammonium hydroxide (25%) and formic acid as described above. The time required for this reaction was 30 minutes at 20°C. The isolated compound gave positive reactions with Tollens' and Fehling's reagents indicating it

be an aldehyde. It was identified as 10-undecenaldehyde (XXI) on

$$CH_2=CH-(CH_2)_8-CHO$$

(XXI)

the basis of its refractive index 1.416 (1.4427)[118,119]. It formed a 2,4-dinitrophenylhydrazone 132-35 °C.

The easy formation of aldehydes from oleic acid and 10-undecenoic acid indicated that isolated double-bonds do not hamper this reaction.

Cinnamaldehyde

It was of interest to examine whether αβ-unsaturated acid chlorides also can undergo this reaction. The αβ-unsaturated double-bond in such aldehydes can undergo addition of hydrogen at the 3-4 site or undergo 1-4 addition followed by the formation of the saturated aldehyde through keto - enol tautomerism of the 1-4 addition product.

It was then decided to examine cinnamic acid (XXII) to check

$$C_6H_5-CH=CH-COOH$$

(XXII)

the direction of this reaction. Cinnamic acid was converted into the chloride by heating with thionyl chloride in chloroform in the presence of catalytic quantity of dimethylformamide. The acid chloride obtained was dissolved in chloroform (20% w/v), covered

with a layer of ammonium hydroxide (25%) and treated with formic acid under nitrogen. The reaction was completed in 50 minutes. The isolated product had the characteristic smell of cinnamaldelyde. It also tested positive with Tollens', Fehling's and Benedict's reagents. The aldehyde was found to be homogeneous when examined by GLC (retention time = 2.95 minutes). The 2,4-dinitrophenylhydrazone of this aldehyde m.p. 202-205 °C (200-202°C) and its refractive index of 1.621 (1.619)[118,119] led to its identification as cinnamaldehyde (XXIII).

$$C_6H_5-CH=CH-CHO$$

(XXIII)

3,3 - Dimethylacraldehyde

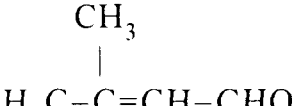
The 3.3 - dimethylacrylic acid (XXIV) which also has similarly

$$H_3C-\underset{\displaystyle CH_3}{\overset{|}{C}}=CH-COOH$$

(XXIV)

situated functionalities as cinnamaldehyde was then examined to confirm that αβ - unsaturated aldehydes can be derived form αβ-unsaturated acid chlorides by this method. The acid chloride of 3,3-dimethylacrylic acid was prepared by heating a solution of this acid

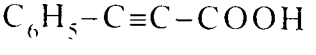
in benzene with thionyl chloride. The acid chloride obtained was dissolved in chloroform (33%; w/v) and treated with formic acid in presence of ammonium hydroxide (25%). The total time required for the reaction was 45 minutes. The product of the reaction was detected to be an aldehyde by its characteristic reactions with Tollens', Fehling's and Benedict's reagents. The GLC examination of this aldehyde in which the retention time was detected to be 2.2 minutes also confirmed its homogenity. It formed a 2,4 -dinitrophenylhydrazone m.p. 155-158°C. Its identity as 3,3-dimethylacraldehyde (XXV) was also established by the determination of its refractive index 1.457 (1.4558)[118,119].



(XXV)

Phenylpropiolaldehyde

While in the previous two instances cited, the αβ - unsaturated acids were found to be easily reduced to the corresponding aldehydes, it was also of interest to examine whether αβ-ynic acid chlorides also shall undergo a similar reaction or not. Hence, the chloride of phenylpropiolic acid (XXVI) was prepared by treating with thionyl



(XXVI)

chloride in refluxing benzene. The chloroformic solution (20%; w/v) of the chloride on the usual treatment with formic acid in presence of ammonium hydroxide (25%) yielded a liquid. This was found to be an aldehyde on the basis of positive reactions towards Tollens', Fehling's and Benedict's reagents. The aldehyde was identified as phenylpropiolaldehyde (XXVII) by determining its refractive index of 1.599 (1.6079)[118,119] and 2,4-dinitrophenylhydrazone 188-90°C.

$$C_6H_5-C\equiv C-CHO$$

(XXVII)

From the last three preparations reported viz: cinnamaldehyde, 3,3-dimethylacraldehyde and phenylpropiolaldehyde it is evident that no type of unsaturation situated αβ- to the acid function interferes in this reaction and the aldehydes obtained in all these cases tested carried αβ - unsaturation.

The results of what are reported above are provided in Table VI. Summarising the results of the preparation of the aldehydes described above, it transpires that :

(a) this method of preparation of aldehydes from acid chlorides is viable and the yields of the aldehydes obtained are uniformly above 75%;

(b) the reagents required for this conversion are commonly accessible and are inexpensive;

TABLE - VI

Aldehydes	Reaction Condition		Characteristics				2,4 Dinitro-phenylhy-drazone	Yield (%)
	Time (min)	Solvent	Tollens' test	Fehling's test	Benedicts' test	Refractive Index		
Propioaldehyde	45	Ether	+ve	+ve	-ve	1.376 [1.3636]	152-156 [155]	79
Butyraldehyde	35	Chloroform	+ve	+ve	-ve	1.411 [1.379]	118-124 [123]	90
Lauraldehyde	25	Chloroform	+ve	+ve	+ve	–	104-108 [106]	96
Palmitaldehyde	20	Chloroform	+ve	+ve	+ve	–	107-110 [105-7]	95
Stearaldehyde	20	Chloroform	+ve	+ve	+ve	–	124-127	94
Benzaldehyde	50	Chloroform	+ve	-ve	+ve	1.522 [1.5456]	235-39 [237]	79
Phenylacet aldehyde	50	Chloroform	+ve	+ve	+ve	1.536 [1.5255]	126-128 [126]	80
Monochloroacet-aldehyde	45	Chloroform	+ve	+ve	+ve	1.435 [1.403]	108-110	82

2-Chloropropion-aldehyde	45	Chloroform	+ve	+ve	-ve	1.441 [1.431]	137 Decomp.	79
Trichloroacet aldehyde [along with chloralhydrate]	50	Chloroform	+ve	+ve	+ve	1.449 [1.45572]	130-34 [131]	76
10-Undecenal-dehyde	30	Chloroform	+ve	+ve	-ve	1.416 [1.4427]	132-35	91
Olealdehyde	30	Chloroform	+ve	+ve	-ve	1.456 [1.4558]	67-70 [67-8]	91
Dimethylacr-aldehyde	45	Chloroform	+ve	+ve	+ve	1.457 [1.4528]	155-58	86
Cinnamaldehyde	50	Chloroform	+ve	+ve	+ve	1.621 [1.619]	202-205 [200-202]	90
Phenylpropiol-aldehyde	50	Chloroform	+ve	+ve	+ve	1.599 [1.6079]	188-190	79
Isobutyraldehyde	25	Chloroform	+ve	+ve	+ve	1.401 [1.372]	188-192 [187]	86
Pivalaldehyde	20	Chloroform	+ve	+ve	+ve	1.398 [1.379]	207-211 [209]	85

Note : a. Yields of aldehydes are as isolated
b. Literature values are given in parentheses.

(c) the reaction conditions are very simple and the exclusion of moisture or low or high temperatures are not required, as is the case with the other comparable methods;

(d) time required for the reaction is small and uniformly less than an hour;

(e) this method is equally applicable to aromatic and aliphatic acid chlorides.

(f) presence of unsaturation, whether isolated or located at αβ-position of the substrate do not hamper this reaction and the corresponding unsaturated aldehydes are obtained in good yields;

(g) halogen containing acid chlorides undergo reduction to the corresponding aldehydes in a facile manner;

(h) primary, secondary and tertiary acid chlorides undergo easy reduction to the corresponding aldehydes and the order of reactivity is tertiary > secondary > primary;

(i) in the fatty acid series, the higher fatty acid chlorides are more reactive than the lower members.

This method, hence, can develop into a general method of preparation of aldehydes. Additionally this process holds the promise of being scaled up as an industrial method.

Mode of reaction

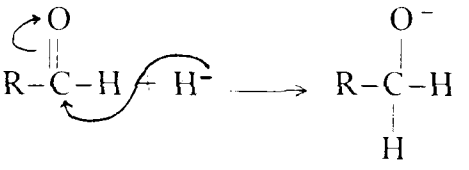
The reaction can be basically considered to be a substitution process in which the chlorine in the substrate is substituted by a

hydride (equation 50). The feasibility of such a reaction taking place

(50)

is extremely likely in case of an acid chloride as the carbonyl carbon is a highly electron deficient centre as it carries two strongly electronegetive atoms. This high electrophilicity would make it highly susceptible to attack by a nucleophile. The facile conversion of the acid chlorides, the most reactive of acid derivatives, to esters, amides and anhydrides are supposed to take place through such nucleophilic substitution processes.

Metal hydrides which are commercially available are the conventional sources of hydrides. Such reagents, however, shall not be successful in this case as the aldehyde which is generated following the nucleophilic substitution can further add a hydride to form an alcohol (equation 51). The reducing agent hence has to be relatively mild in character in order to stop the reaction at the substitution



(51)

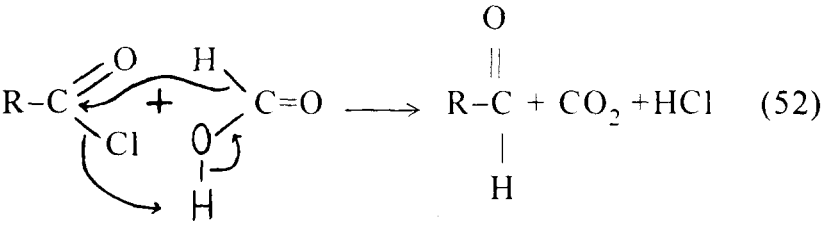
stage. Several metal hydrides like $LiAlH_4$ and $NaBH_4$ have been modified to reduce its activity. One such modified reagent is lithium -tri-t-butoxyaluminium hydride (XXVIII). Expectedly this reagent has

$LiAl(t\text{-}OC_4H_9)_3H$

(XXVIII)

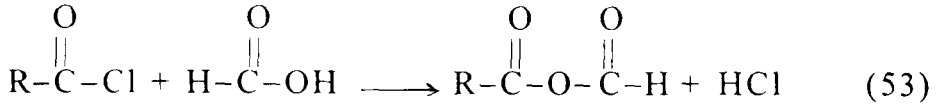
been found to reduce acid chlorides to aldehydes. This reduction can be carried out in diglyme, the preferred temperature being 0°C. The reaction in this case stops at the aldehyde stage because of steric hindrance.[51]

The idea which gave rise to this reaction was the possibility of using formic acid as a hydride donor which could interact with an acid chloride through a cyclic transition state (equation 52). This

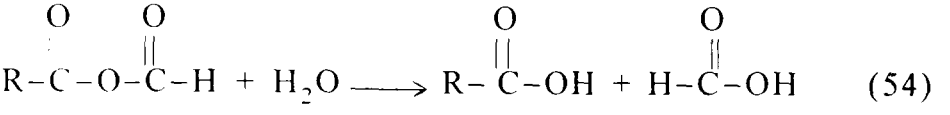


(52)

possibility when examined experimentally, with formic acid and an acid chloride gave no aldehyde. Probably what was generated was a mixed anhydride which hydrolysed during work up (equation 53 and 54).



(53)

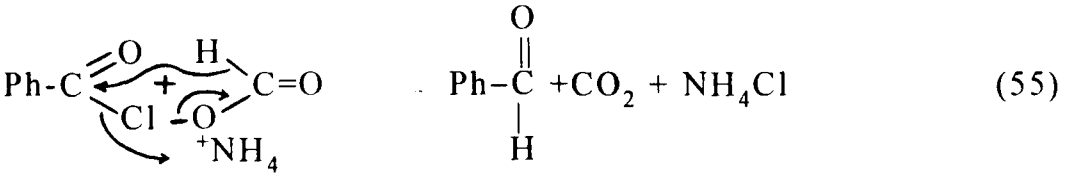


(54)

As explained earlier, in order to minimise the contact between the reactants which otherwise leads to the formation of anhydrides, it was thought desirable to have the two reactants in two different phases and stir them to bring the reactants into contact. Benzoyl chloride was thus dissolved in chloroform and formic acid in water. Prolonged stirring of this mixture (over 6 hours) resulted in the formation of benzaldehyde in an yield of 20%.

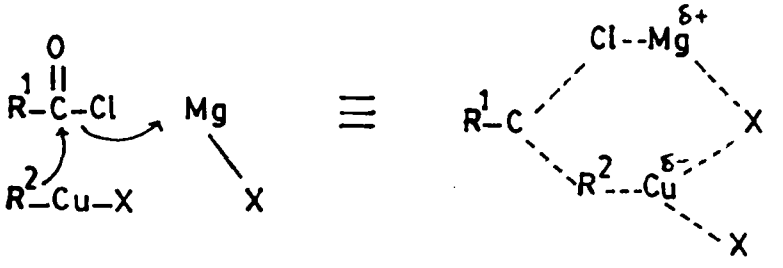
It was then decided to approach this reaction from a different angle, by adopting the Schotten - Baumann conditions. Water was then substituted by aqueous base. Addition of formic acid to aqueous base shall result in the formation of the salt of formic acid. The cation can attract the chlorine of the acid chloride away from the carbon. This further electron depletion from the carbonyl carbon can increase the electrophilicity of the carbonyl carbon facilitating the attack by a nucleophile on this carbon. Such a syndrome has been classified as a push - pull machanism[117].

Under these altered conditions, wherein benzoyl chloride in chloroform reacts with formic acid in ammonium hydroxide, and assuming the reaction to proceed, again, through a cyclic process the reaction can be depicted as below (equation 55). Benzaldehyde in this case was obtained in an yield of 79%.



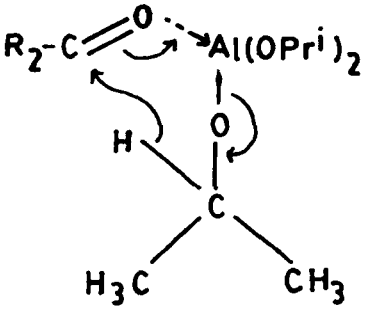
(55)

Such a cyclic transition state (XXIX) has been reported in the formation of ketones in the reaction between an acid chloride and a Grignard reagent in presence of cuprous chloride[121].



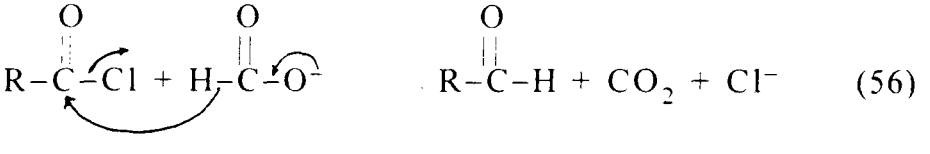
(XXIX)

Though not exactly analogous the reduction of carbonyl compounds by the Meerwein-Ponndorf - Verley reduction has also been postulated to take place through a cyclic transition state (XXX)[122].



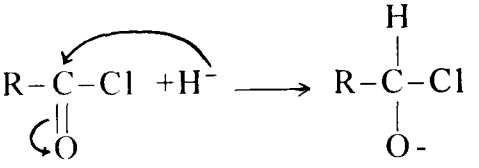
(XXX)

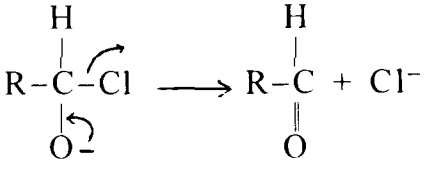
However an opinion persists that concerted displacement at sp^2 centres are not usually valid[123]. If this opinion is taken to be correct, one of the alternatives shall be as below (equation 56), though in this case the competitive reaction involving the nucleophilic attack by the acid anion on the carbonyl carbon should exist with the formation of some quantity of the anhydride.



(56)

Another pathway could involve a tetrahedral mechanism[124] (equation 57) which in this instance can be interpreted as below, involving addition of the hydride and the departure of the halide.





(57)

Whatever may be the actual path through which this reaction proceeds. the decomposition of the formate has to result in the liberation of CO_2. Similarly the expulsion of chloride has to take place from the acid chloride. These aspects were checked and the GLC examination of the gases generated during the reaction was found to contain CO_2. The identity of CO_2 was confirmed by comparison with a standard sample. The aqueous solution obtained after removal of the chloroform layer was acidified with dilute HNO_3 followed by addition of silver nitrate. A copious precipitate which was thus obtained was soluble in excess of ammonia. The precipitate did not show any change in colour to grey followed by black as would have been the case had the precipitate been silver formate. The postulated products of the reaction, CO_2 and chloride having been thus identified. whatever may be the reaction pathway. it is clear that formic acid is being oxidised to CO_2 and the acid chloride reduced to the aldehyde.

REDUCTION OF ACID CHLORIDES TO ALDEHYDES BY CATALYTIC TRANSFER HYDROGENATION

CATALYTIC TRANSFER HYDROGENATION

CATALYTIC TRANSFER HYDROGENATION

Catalytic hydrogenation is probably the most commonly used method of reduction in organic chemistry. It is effected by treating a solution of a compound with a heterogenous catalyst in presence of hydrogen. Variables in this process are catalysts and solvents. More recently availability of soluble catalysts have made it possible to carry out the hydrogenation in a homogenous system. Hydrogenation can result in addition of hydrogen to the substrate or hydrogenolysis.

Transfer hydrogenation differs from the classical catalytic hydrogenation in that gaseous hydrogen is not used and instead certain chemicals are used which donate hydrogen to the substrate resulting in addition or hydrogenolysis. This method has the advantage of not having to use gaseous hydrogen and the consequent prevention of the likely hazards. The substance which donates hydrogen to the substrate is known as the donor. The substrate which accepts hydrogen is known as the acceptor.

Though sporadic reports have been made earlier citing examples of transfer hydrogenation, it was only 1952 that systematic studies were taken up to develop this method[125]. It was reported that ethylenic and acetylenic bonds can be reduced by refluxing with cyclohexene in tetrahydrofuran in presence of platinum black as the catalyst. In this reaction cyclohexene is the donor and unsaturated compounds the acceptor. As in the case of catalytic hydrogenation in this process also homogenous catalysts have been successfully tried out[126,127]. Carbon-carbon double bonds located in hydrocarbons, acids, ketones, aldehydes, esters and nitriles have been successfully reduced by this method. Though the carbonyl group is resistant to reduction, when Raney-nickel is used as a catalyst with alcohol as the donor, it also has been reduced to methylene.

Hydrogenolysis have also been achieved by transfer hydrogenation. The carbon-nitrogen triple bond is normally reduced to a methyl group. Halogens in organic compounds also undergo hydrogenolysis including those bound to an aromatic ring. Allylic and benzylic functions also expectedly undergo hydrogenolysis by this method.

In spite of the easy reducibility of acid chloride and the apparent reluctance of the carbonyl group to undergo reduction only one case of the reduction of an acid chloride to an aldehyde had been reported and that too in very small yield[128].

Catalytic transfer hydrogenation has been [illegible] by G. Brieger and T. J. Nestrick in the Chemical Reviews[129]. They have systematically

classified the effects of the variables involved in this reaction, which can be summarized as below.

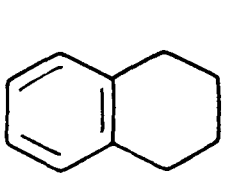
1. **Solvent** - Certain terpenes, aromatic hydrocarbons, lower fatty acids, alcohols, ethers and amines have been variously used as solvent. Gaiffe and Plotiau[130], have reported the particular efficiency of tetrahydrofuran as a solvent. The choice of alcohol as a solvent has to be made carefully as it can also act as a hydrogen donor. Another aspect to be considered is the temperature at which the reaction has to be carried out, because the donors are reluctant to act below a critical temperature which are specific for different donors.

2. **Catalyst** - It appears that the maximum work, on catalysts have been done on palladium. Various forms of palladium used are Pd-Black, Pd/C, Pd/Alumina, 10% Pd/C, 1% Pd/$CaCO_3$, 0.1% Pd/Al_2O_3, Pd Cl_2 or Pd/Pt. In a study on the hydrogenation of p-nitrotoluidine it was observed that Pd-catalysts are more effective than others.

Raney - nickel is another catalyst which has been widely used. Additionally, catalysts used for transfer hydrogenation are the ruthenium complex $RuCl_2(Ph_3P)_3$[127], the iridium complexes $IrHCl_2(Me_2SO)_3$[126,129,131], $Ir(CO)Br(Ph_3P)_2$[132], the rhodium complex $RhCl(Ph_3P)_3$[132] and the platinum complex $PtCl_2(Ph_3As)_2$ with $SnCl_2.H_2O$.[133]

3. **Temperature** - Normally the temperature depends upon the donor, though at higher temperature the reaction cannot be controlled and it has been observed that even benzene can be totally hydrogenated intocyclohexane.[134]

4. **Donor** - The choice of donor is generally determined by the ease of reaction, solubility of the substrate and availability. Cyclohexene is a preferred donor because of its ready availability and high reactivity. Tetralin (XXXI), the readily available monoterpenes, limonene(XXXII), terpinolene(XXXIII) or α-phellandrene(XXXIV) are also used commonly.



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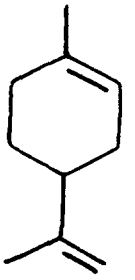

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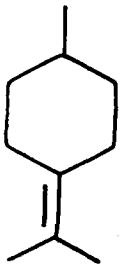
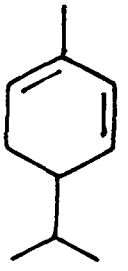


(XXXIII)



(XXXIV)

However, where reduction of carbonyl groups are required alcohols are the donors of choice. In the review by Brieger G. and Nestrick T.J.[129] formic acid has been shown to have very low preference and that too preferably when soluble catalyst are used in conjuction. However, formic acid has been reported to be an effective donor for hydrogenolysis of benzyl type protecting groups from peptide.[135]

In continuation with our earlier work reported on the conversion of acid chlorides to aldehydes, we decided to explore the possibility of modifying the Rosenmund reduction by employing transfer hydrogenation using formic acid as donor, in lieu of catalytic hydrogenation. The success of this approach would have depended upon the catalyst.

Most of the catalysts reported to be used except the homogenous complex ones are readily available in the market and mainly are of standard compositions. In the proposed reduction of acid halides to aldehydes the most commonly used catalyst of Pd has not been found to be successful[128]. It was thought desirable therefore to prepare other catalysts and alter the composition to suit this purpose.

In the context of this reaction our attention was attracted to the Urushibara nickel catalyst (abbreviated as U-Ni) discovered by Urushibara and Chuman[136]. This work was followed up by K. Sakai et al who examined the catalytic characteristics of the precipitated nickel, a precusor of theU-Ni.[137] They also examined other precipitated metals (abbreviated as ppt-metals) and mixed precipitated metals, beside providing details of preparation and properties of such catalysts. Activities of the catalysts examined were graded and were reported as ppt - Ni - Co > ppt - Ni > ppt - Ni - Fe > ppt - Co > ppt - Ni - Cu > ppt - Cu > ppt - Fe, suggesting that the activity of catalyst can be modulated by choosing the proper combination of metals. However, they had stated that to carry out reduction by these catalysts water was indispensable as a hydrogen donor.

Assuming that the polarity of water is what makes it indispensible to carry out reduction with these catalysts, we decided to examine these precipitated metals in presence of formic acid. The precipitated Ni and Cu catalysts were therefore prepared and acid chloride treated with formic acid in presence of trimethylamine as an acid scavenger. There was no perceptible reaction when the acid chloride and formic acid were mixed together, but immediately on addition of the catalyst there was brisk effervescence. On slowing down of this effervescence the mixture was warmed on the water bath for varying degrees of time. Final work up of this mixture showed that aldehydes were indeed formed. Several aldehydes were prepared by this method as described subsequently.

CURRENT WORK

CURRENT WORK :

Synthesis of Aldehydes by catalytic transfer hydrogenation

Benzaldehyde

Formic acid (2.76 gm) and excess trimethylamine were taken in a round bottomed flask and to this gradually added a solution of benzoyl chloride (2 gm) in benzene (10ml) not allowing the temperature to rise very high. To this mixture, cooled to room temperature was added 1 gm of ppt-Ni catalyst (Ni : Zn ; 1:1) with continuous stirring. A vigorous reaction ensued and after the evolution of the gas subsided the whole mixture was heated for 1 hour. The catalyst was filtered off from the reaction mixture and the filtrate washed with water and the benzene solution so obtained dried over anlydrous sodium sulphate. To this dry benzene solution was added 2,4 - dinitrophenylhydrazine hydrochloride and the hydrazone formed filtered, dried and crystallized from alcohol. The yield calculated on the basis of the phenylhydrazone was found to be 73%.

With use of ppt-Cu catalyst (Zn : Cu ; 1 : 1), the basic procedure was the same except that the reaction mixture was heated for 1.5 hours. The yield obtained in this case was 76%.

Butyraldehyde

Using basically the same procedure butyryl chloride was treated with formic acid and trimethylamine in benzene in presence of ppt-Ni catalyst for 1 hour. The aldehyde formed isolated in the form of 2,4-dinitrophenyhydrazone was obtained in 66% yield.

When ppt-Cu catalyst was used the time required was 1.5 hours and the yield of the aldehyde 70%.

Isobutyraldehyde

The isobutyryl chloride was slightly more sluggish to react and in presence of ppt-Ni catalyst, the time required was 1.5 hours. The aldehyde was obtained in an yield of 75%. With ppt-Cu catalyst the reaction had to be run for 2 hours, and the yield of the aldehyde formed was 77%.

Pivalaldehyde

In the reduction of pivaloyl chloride by formic acid in presence of ppt - Ni catalyst the time required for the reaction was 1.5 hours and the yield 77%. With the ppt - Cu catalyst 2 hours were required to complete the reduction. The yield of pivalaldehyde was 81%.

Stearaldehyde

In order to check the probability of reduction of higher fatty acid chlorides, the stearic acid chloride was reduced by using ppt - Ni catalyst over a period of 1 hour. The aldehyde was obtained in an yield of 81%. The ppt - Cu catalyst was effective though the duration of the reaction was 2 hours. In this case the yield was better at 86%.

Reduction of unsaturated Acid Chloride - Oleoyl Chloride

In order to examine whether double bond will be affected by this reducing agent or not, oleoyl chloride was treated with formic acid in presence of ppt - Ni catalyst. As was observed in previous cases there was brisk evolution of CO_2 and the reaction was completed in 1 hour. When ppt-Cu catalyst was used the reaction took 2 hours for completion. Aldehydes obtained in both cases formed the same 2,4-dinitrophenyl-hydrazone which was identified as the 2,4-dinitrophenylhydrazone of stearaldehyde. Yields obtained in the former case was 83% and in the latter 74%. It is hence apparent that the double bond in oleic acid is hydrogenated along with the hydrogenolysis of the C-Cl bond of the acid chloride.

Cinnamoyl Chloride

Oleic acid carries an isolated double bond which is reduced under the reaction conditions. It was therefore thought proper to examine an α,β-unsaturated acid chlorideas well. Accordingly cinnamoyl chloride was reduced with formic acid in presence of ppt-Ni and ppt-Cu catalysts.

Time required in the former case was 1 hour and in the latter 2 hours. Yields obtained with ppt-Ni catalyst was 78% and ppt-Cu catalyst 73%. Product obtained in both these runs were identical and gave the same 2.4-dinitrophenylhydrazone m.p. 150-154°C (151-152)[118,119], though not of cinnamaldehyde. A survey of literature made it possible to identify the aldehyde hydrocinnamaldehyde.

It is evident from the above discussion that -

1. Transfer hydrogenation can be used instead of catalytic hydrogenation for the Rosenmund reduction of acid chlorides.
2. The precipitated metal catalysts are effective in the preparation reduction listed above.
3. Precipitated metal catalyst of varying compositions can be prepared very conveniently in the laboratory.
4. Though the activities of the catalysts used have been classified as ppt-Ni > ppt-Cu[137], in this reaction better yields were obtained with ppt-Cu catalyst except in the cases of unsaturated aldehydes. As can be expected with acid chlorides which are very easily reducible, a milder catalyst should give better yields while a stronger catalyst can cause over-reduction.
5. Based on the preparation of seven aldehydes listed above it can be concluded that
   (a) primary, secondary, tertiary and aromatic acid chloride can be conveniently reduced to aldehydes in very good yields.

(b) The double bond present in unsaturated acid chlorides, whether isolated or conjugated, are concomintantly hydrogenated to give rise to saturated aldehydes.

Summary of the experiments performed using catalytic transfer hydrogenation is provided in the table VII.

TABLE - VII

Acid chloride	Reaction Time (Catalyst)		Solvent	Product obtained (Aldehyde)	% yield of 2,4-Dinitrophenylhydrazone	
	ppt-Ni	ppt-Cu			ppt-Ni	ppt-Cu
Benzoyl chloride	1 hour	1.5 hours	Benzene	Benzaldehyde	73	76
Butyryl chloride	1 hour	1.5 hours	Benzene	Butyraldehyde	66	70
Isobutyryl chloride	1.5 hours	2 hours	Benzene	Isobutyraldehyde	75	77
Pivaloyl chloride	1.5 hours	2 hours	Benzene	Pivalaldehyde	77	81
Stearic acid-chloride	1 hour	2 hours	Benzene	Stearaldehyde	81	86
Oleoyl chloride	1 hours	2 hours	Benzene	Stearaldehyde	83	74
Cinnamoyl chloride	1 hours	2 hours	Benzene	Hydrocinnamal-dehyde	78	73

EXPERIMENTAL

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. IR spectra were recorded in KBr/Nujol/neat on a IR-408 Shimadzu spectrophotometer. ^{1}H-NMR were determined on Hitachi Perkin Elmer (80 MHz) instrument in $CDCl_3$ using TMS as internal standard, and chemical shifts recorded in δ values relative to TMS assigned at zero. The refractive indices were measured on Abbe refractometer using visible light (electric bulb) with temperature maintained at 20-25 °C. Slight deviations in the observed values in relation to the reported ones are thus explained.

The Gas chromatograms were determined on a Nucon Gas Chromatograph using a glass column of carbowax-200 C maintaining the oven temperature above the boiling point of the aldehydes. TLC were carried on silica gel G_{254} (E. Merck). Iodine or 2,4-dinitrophenylhydrazine were used for visualization of TLC plates.

The aldehydic reagents - Tollens', Fehling's and Benedict's used for testing prepared aldehydes were of Analytical reagent grade (BDH or Qualigen).

General experimental procedure - Preparation of acid chlorides

The acid chlorides were prepared by standard methods from the corresponding acids. The acid (O.1 M) was dissolved in benzene or chloroform (20 ml) and to this thionyl chloride (0.15 M) added. Where required dimethylformamide was used as a catalyst. The mixture was refluxed for varying degrees of time till the evolution of HCl ceased. The solvent was evaporated to give the acid chloride which was distilled before used.

Derivatisation

Phenylhydrazone- Phenylhydrazine hydrochloride solution was prepared by dissolving phenylhydrazine in ethanol and concentrated HCl added to it. The solid phenylhydrazine hydrochloride obtained thus was crystallised. Phenylhydrazine hydrochloride (5 gm) and sodium acetate (8 gm) were dissolved in water (50 ml) to obtain a stock solution. To an aliquot of this solution an alcoholic solution of the aldehyde was added and stirred till a clear solution was obtained. The whole mixture was warmed on water bath for 20 minutes, cooled and filtered to obtain a solid which was crystallised from ethanol.

2,4 - Dinitrophenylhydrazone - To the clear solution obtained by warming 2,4-dinitrophenylhydrazine. HCl (1 ml) and ethanol (8-10 ml) the aldehydic solution was added and the mixture heated to boil. This

mixture was cooled and filtered to obtain the solid 2,4-dinitrophenylhydrazone which was crystallised from ethanol .

General experimental procedure for aldehyde synthesis :

The prepared acid chloride (3-5 gm) was dissolved in chloroform (15 ml) and the solution deoxygenated by bubbling N_2 through the solution. This solution was covered by ammonium hydroxide (25%) followed by gradual addition of formic acid (excess : three fold over acid chloride), the whole mixture being stirred for varying degrees of time under N_2. The reaction was monitored on the basis of evolution of CO_2. When the CO_2 evolution ceased, the reaction mixture was stirred for another 5 minutes. The organic layer was separated washed with water and dried over anhydrous sodium sulphate ($Na_2 SO_4$). The product was obtained by evaporating the solvent under nitrogen to prevent the possible aeriel oxidation of aldehyde formed.

Tests for Aldehydes

I. **Tollens' Test** - 2 ml of Tollens' reagent along with few drops of isolate was shaken well and heated on a water bath. A silver - mirror or a greyish black ppt confirmed the presence of the aldehyde function.

II. **Fehling's Test** - 1ml of isolated solution together with 2 ml of freshly prepared Fehling's solution obtained by mixing 1 ml of Fehling's solution A with 1 ml of Fehling's solution B was warmed. A positive response was indicated by the appearance of a red precipitate.

III. **Benedict's Test** - 5 ml of Benedict's reagent along with 0.5 ml of isolated solution was heated together directly on a flame. A red / yellow / green colour indicated a positive response.

Benzaldehyde

1. **Reactants :** Benzoyl Chloride (4 gm; 0.028 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), formic acid (4.6 gm; 0.1 M), reaction time 50 minutes, Yield 79%

Tollens' test : Positive

Fehling's test : Negative

Benedict's test : Positive

Refractive index : 1.522

Phenylhydrazone mp : 156 - 58°C

2,4 - Dinitrophenylhydrazone mp : 235 - 39°C

GLC (Solvent: chloroform) : Retention time 4 minutes

IR (KBr) υ_{max} : 1705 cm^{-1} (C=O)

^{1}H-NMR ($CDCl_3$) : δ 7.5 (m, 3H), 7.75 (m, 2H), 9.95 (s,1H)

2. **Reactants :** Benzoyl Chloride (4 gm; 0.028 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), sodium formate (6.8 gm; 0.1 M) in distilled water (5 ml); reaction time 50 minutes, Yield 75%

Tollens' test : Positive

Fehling's test : Negative

Benedict's test : Positive

Refractive index : 1.522

Phenylhydrazone mp : 156 - 58°C

2,4 - Dinitrophenylhydrazone mp : 235 - 39°C

GLC (Solvent; chloroform) : Retention time 4 minutes

3. Reactants : Benzoyl Chloride (4 gm; 0.028 M) in chloroform (15 ml), 0.3 M sodium hydroxide aqueous solution (30 ml) formic acid (4.6 gm; 0.1 M): reaction time 30 minutes. Yield 72%

Tollens' test : Positive

Fehling's test : Negative

Benedict's test : Positive

Refractive index : 1.522

Phenylhydrazone mp : 156 - 58°C

2.4 - Dinitrophenylhydrazone mp : 235 - 39°C

GLC (Solvent; chloroform) : Retention time 4 minutes

Propionaldehyde

Reactants : Propionoyl chloride (3 gm: 0.033 M) in diethylether (15 ml): ammonium hydroxide (25%: 30 ml), formic acid (4.6 gm : 0.1 M) : reaction time 45 minutes, yield 79%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Negative

Refractive index : 1.376

2.4 - Dinitrophenylhydrazone mp : 152 - 56°C

GLC (Neat) : Retention time 1.8 minutes

IR (KBr) ν_{max} : 1710 cm^{-1} (C=O)

^{1}H-NMR ($CDCl_3$) : δ 10.1(1H.s), 2.7 (2H.t), 1.6(2H.m),0.97(3H,t)

Butyraldehyde

Reactants : Butyryl chloride (3 gm; 0.028M) in chloroform (15 ml), ammonium hydroxide (25%; 30ml), formic acid (4.6 gm; 0.1 M) ; reaction time 35 minutes, yield 90%.

Tollens' test : positive

Fehling's test : positive

Benedict's test : Negative

Refractive index : 1.411

2.4 - Dinitrophenylhydrazone mp : 118 -24°C.

GLC (solvent : $CHCl_3$) : Retention time 6.12 minutes

Phenylacetaldehyde

Reactants : Phenylacetyl chloride (5 gm : 0.032 M) in chloroform (15 ml), ammonium hydroxide (25% : 30 ml), formic acid (4.6 gm: 0.1M); reaction time 50 minutes, yield 80%.

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.536

2,4 - Dinitrophenylhydrazone mp : 126 - 28°C.

GLC (solvent : $CHCl_3$) : Retention time 3.68 minutes

Isobutyraldehyde

Reactants : Isobutyryl chloride (4 gm; 0.037 M) in chloroform (15ml), ammonium hydroxide (25%; 30 ml), formic acid (5.32 gm; 0.12M), reaction time 25 minutes, yield 86%.

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.401

2,4 - Dinitrophenylhydrazone m.p. : 188 - 92°C

GLC (solvent : $CHCl_3$) : Retention time 4.72 minutes.

Pivalaldehyde

Reactants : Pivaloyl chloride (4gm; 0.033 M) in chloroform (15 ml), ammonium hydroxide (25% : 30 ml), formic acid (4.6 gm : 0.1 M) ; reaction time 20 minutes, yield 85%.

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.398

2,4 - Dinitrophenylhydrazone (mp.) : 207-211°C

Monochloroacetaldehyde

Reactants : Chloroacetyl chloride (4 gm ; 0.035 M) in chloroform (15 ml), ammonium hydorxide (25% ; 30 ml), formic acid (4.6 gm ; 0.1 M); reaction time 45 minutes, yield 82%.

Tollens' test : Positive

Fehling's test : positive

Benedict's test : Positive

Refractive index : 1.435

2,4 - Dinitrophenylhydrazone mp : 108 -110°C

GLC (solvent : $CHCl_3$) : Retention time 4.2 minutes.

2- Chloropropionaldehyde

Reactants : 2-chloropropionoyl chloride (4 gm; 0.031 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), formic acid (4.6 gm; 0.1 M); reaction time 45 minutes, yield 79%.

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Negative

Refractive index : 1.441

2,4-Dinitrophenylhydrazone mp : 137 °C decomp.

GLC (solvent : $CHCl_3$) : Retention time 6.8 minutes.

Trichloroacetaldehyde

Reactants : Trichloroacetyl chloride (4 gm, 0.022 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), formic acid (3.25 gm; 0.07 M); reaction time 50 minutes; yield 76% as trichloroacetaldehyde and chloralhydrate.

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.449

2,4-Dinitrophenylhydrazone mp : 130-34 °C

GLC (solvent : $CHCl_3$) : Retention time 2.28 minutes.

Chloralhydrate mp : 53 °C

Lauraldehyde

Reactants : Lauroyl chloride (4 gm; 0.018 M) in chloroform (15 ml), ammonium hydroxide (25%, 30 ml), formic acid (2.75 gm; 0.06 M); reaction time 25 minutes, m.p. 43-46 °C, Yield 96%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

2,4-Dinitrophenylhydrazone mp : 104-108 °C

TLC (silicagel : G_{254}) Solvent : Petroleum ether : Ethylacetate : Acetic acid (70 : 30 : 1); $R_f = 0.08$

Palmitaldehyde

Reactants : Palmitic acid chloride (4 gm; 0.014 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), formic acid (1.9 gm; 0.042 M); reaction time 20 minutes; mp 35°C, yield 95%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

2,4-Dinitrophenylhydrazone mp : 107-110 °C

TLC (silicagel : G_{254}) Solvent : Petroleum ether : Ethylacetate : Acetic acid (70 : 30 : 1); R_f = 0.073

Stearaldehyde

Reactants : Stearic acid chloride (4 gm; 0.013 M) in chloroform (15 ml); ammonium hydroxide (25%; 30 ml), formic acid (1.9 gm; 0.042 M); reaction time 20 minutes, mp 57°C, yield 94%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

2,4-Dinitrophenylhydrazone mp : 124-127 °C

TLC (silicagel : G_{254}) Solvent : Petroleum ether : Ethylacetate : Acetic acid (70 : 30 : 1); R_f = 0.65

Olealdehyde

Reactants : Oleoyl chloride (4 gm; 0.013 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), formic acid (1.9 gm; 0.042 M) reaction time 30 minutes, yield 91%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Negative

Refractive index : 1.456

2,4-Dinitrophenylhydrazone mp : 67-70 °C

TLC (silicagel : G_{254}) Solvent : Petroleum ether : Ethylacetate : Acetic acid (70 : 30 : 1); $R_f = 0.58$

10-Undecenaldehyde

Reactants : 10-undecenoyl chloride (4 gm; 0.018 M) in chloroform (15 ml), ammonium hydroxide (25%; 30 ml), formic acid (2.75 gm; 0.06 M); reaction time 30 minutes, yield 91%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Negative

Refractive index : 1.416

2,4-Dinitrophenylhydrazone mp : 132-35 °C

TLC (silicagel : G_{254}) Solvent : Petroleum ether : Ethylacetate : Acetic acid (70 : 30 : 1); $R_f = 0.50$

Cinnamaldehyde

Reactants : Cinnamoyl chloride (3 gm; 0.018 M) in chloroform (15 ml), ammonium hydroxide (25 %; 30 ml), formic acid (2.5 gm; 0.054 M); reaction time 50 minutes, yield 90%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.621

2,4-Dinitrophenylhydrazone mp : 202-205 °C

GLC (solvent : $CHCl_3$) : Retention time 2.95 minutes.

3,3-Dimethylacraldehyde

Reactants : Dimethylacroyl chloride (5 gm; 0.042 M) in chloroform (15 ml), ammonium hydroxide (25 %; 30 ml), formic acid (6.0 gm; 0.13 M); reaction time 45 minutes, yield 86%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.457

2,4-Dinitrophenylhydrazone mp : 155-58 °C

GLC (solvent : $CHCl_3$) : Retention time 2.2 minutes.

Phenylpropiolaldehyde

Reactants : Phenylpropiolic acid chloride (3 gm; 0.018 M) in chloroform (15 ml), ammonium hydroxide (25 %; 30 ml), formic acid (2.5 gm; 0.054 M); reaction time 50 minutes, yield 79%

Tollens' test : Positive

Fehling's test : Positive

Benedict's test : Positive

Refractive index : 1.599

2.4-Dinitrophenylhydrazone mp : 188-90 °C

CATALYTIC TRANSFER HYDROGENATION

Preparation of precipitated-metal catalyst : ppt-Ni and ppt-Cu

Zinc dust (10 gm) and distilled water (3 ml) were placed in an Erlenmeyer flask and heated on water bath. An aqueous solution (10 ml) containing either 4.04 gm of nickel(II)chloride ($NiCl_2.6H_2O$) or 2.69 gm of copper(II) chloride ($CuCl_2.6H_2O$), previously heated to 60 °C, was added to the heated zinc dust mud with vigorous shaking. A violent reaction took place, depositing the Ni or Cu on the surface of the zinc dust. The whole solid was collected on a glass filter by suction, washed with water three times and then with methanol and ether and dried under reduced pressure. The precipitated metal catalyst obtained thus contains about 1 gm of each metal, supported on zinc dust.

General Reduction procedure

Formic acid and excess trimethylamine were taken and to this, the solution of acid chloride in benzene (10 ml) added. The molar ratio of formic acid and acid chloride taken were 4:1. Temperature of the mixture was maintained at room temperature by cooling. 1 gm each of the ppt metal catalyst of either Ni or Cu was added to the above solution with continuous stirring, when a vigorous reaction took place with the effervescence. After evolution of the gas had ceased, the reaction mixture was heated on water bath for varying degrees of time. The catalyst was filtered and the filtrate washed with water and dried over anhydrous sodium sulphate (Na_2SO_4). An alcoholic solution of 2,4-dinitrophenylhydrazine hydrochloride was added to the benzene solution and 2-4-dinitrophenylhydrazone formed was filtered, dried and crystallized from ethanol. Yields were calculated on the basis of the phenylhydrazone formed.

Benzaldehyde

Reactants : Benzoyl chloride (2 gm; 0.014 M) in benzene (10 ml), formic acid (2.76 gm, 0.06 M), trimethylamine (4 ml), ppt-Ni or ppt-Cu catalyst (1 gm). Reaction time for ppt-Ni catalyst : 1 hour; Yield 73% and for ppt-Cu catalyst: 1.5 hours, Yield 76%

2,4-Dinitrophenylhydrazone mp : 235-38 °C.

Butyraldehyde

Reactants : Butyryl chloride (2 gm ; 0.019 M) in benzene (10 ml), formic acid (3.70 gm ; 0.08 M), trimethylamine (4 ml), ppt- Ni or ppt-Cu catalyst (1 gm). Reaction timefor ppt-Ni catalyst ; 1 hour, yield 66% and for ppt-Cu catalyst : 1.5 hours, yield 70%.

2,4 - Dinitrophenylhydrazone mp : 120-5°C.

Isobutyraldehyde

Reactants : Isobutyryl chloride (2 gm ; 0.019 M) in benzene (10 ml), formic acid (3.70 gm ; 0.08 M), trimethylamine (4 ml), ppt-Ni or ppt-Cu catalyst (1 gm). Reaction timefor ppt - Ni catalyst : 1.5 hours, yield 75% and for ppt - Cu catalyst : 2 hours, yield 77%.

2,4 - Dinitrophenylhydrazone mp : 186-90°C.

Pivalaldehyde

Reactants : Pivaloyl chloride (2 gm ; 0.016 M) in benzene (10 ml); formic acid (3.22 gm ; 0.07 M), trimethylamine (4 ml), ppt - Ni or ppt-Cu catalyst (1 gm). Reaction time for ppt - Ni catalyst : 1.5 hours, yield 77% and for ppt-Cu catalyst : 2 hours, yield 81%

2,4 - Dinitrophenylhydrazone mp : 204-208°C.

Stearaldehyde

Reactants : Stearic acid chloride (2 gm : 0.006 M) in benzene (10 ml), formic acid (1.38 gm ; 0.03 M), trimethylamine (4 ml), ppt-Ni or ppt-Cu

catalyst (1 gm). Reaction time for ppt - Ni catalyst : 1 hour, yield 81% and for ppt-Cu catalyst : 2 hours, yield 87%.

2,4 - Dinitrophenylhydrazone mp : 123-27°C.

Reduction of Oleoyl chloride

Reactants : Oleoyl chloride (2 gm ; 0.006 M) in benzene (10 ml), formic acid (1.38 gm : 0.03 M) trimethylamine (4 ml), ppt - Ni or ppt-Cu catalyst (1 gm). Reaction time for ppt-Ni catalyst : 1 hour, yield 83% and for ppt-Cu catalyst : 2 hours, yield 74%.

2,4 - Dinitrophenylhydrazone mp : 125-7°C.

Reduction of Cinnamoyl choride

Reactants : Cinnamoyl chloride (2 gm : 0.012 M) in benzene (10 ml), formic acid (2.76 gm : 0.06 M), trimethylamine (4 ml), ppt-Ni or ppt-Cu catalyst (1 gm). Reaction time for ppt-Ni catalyst : 1 hour, yield 78% and for ppt-Cu catalyst : 2 hours, yield 73%.

2,4 - Dinitrophenylhydrazone mp : 150-54°C.

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NEW METHODS FOR SYNTHESES OF ALDEHYDES FROM NATURALLY OCCURRING AND SYNTHETIC ACIDS

SUMMARY

THESIS

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BY

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SUMMARY

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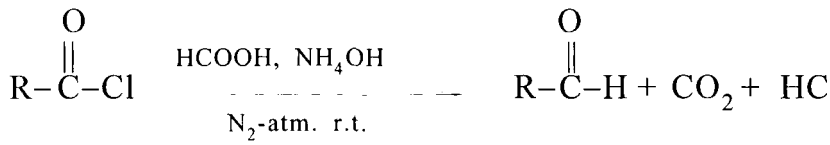
This thesis reports two new methods of synthesis of aldehydes, starting with acid chlorides, The first of this consists of the reduction of acid chlorides by formic acid (Scheme - I). This reduction is effected by

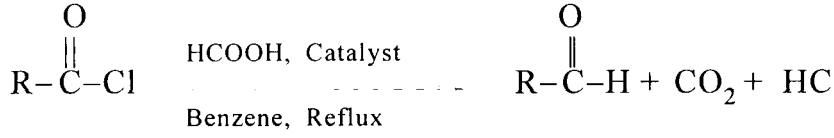


Scheme I

treatment of the solution of the acid chlorides in chloroform by formic acid under basic conditions, at pH - 10. The reduction is carried out at 20 - 30 oC and the reaction time is uniformly less than an hour. Aldehydes are obtained in good to excellent yields ranging from 79 -96%. Primary, secondary, tertiary, long chain aliphatic, aromatic, αβ- unsaturated, αβ acetylenic and halogen containing aldehydes have been prepared by this method, details of which are provided in Table. I

The second method also uses formic acid as a reductant, but the reduction is achieved by catalytic transfer hydrogenation, wherein formic acid acts as the hydrogen donor. Catalysts empolyed in this reaction are

precipitated metals (ppt - Ni and ppt -Cu), a less familiar type of catalyst which can be easily prepared in the laboratory and whose composition can also be varied conveniently. This method thus amounts to a modified Rosenmund reduction (Scheme - II). The reaction is conducted in



Scheme II

refluxing benzene and the reaction time varies from 1 - 2 hours. In this method, however, double bonds if present in the substrate are concomitantly reduced. Yields of the aldehydes obtained in this reaction are exceptionally good and vary from 66 - 83% as detailed in Table - II

TABLE - I

Synthesis of aldehydes from acid chlorides using formic acid as a hydride donor.

Aldehydes	Reaction Condition		Characteristics				2,4 Dinitro-phenylhy-drazone	Yield (%)
	Time (min)	Solvent	Tollens' test	Fehling's test	Benedicts' test	Refractive Index		
Propioaldehyde	45	Ether	+ve	+ve	-ve	1.376 [1.3636]	152-156 [155]	79
Butyraldehyde	35	Chloroform	+ve	+ve	-ve	1.411 [1.379]	118-124 [123]	90
Lauraldehyde	25	Chloroform	+ve	+ve	+ve	–	104-108 [106]	96
Palmitaldehyde	20	Chloroform	+ve	+ve	+ve	–	107-110 [105-7]	95
Stearaldehyde	20	Chloroform	+ve	+ve	+ve	–	124-127	94
Benzaldehyde	50	Chloroform	+ve	-ve	+ve	1.522 [1.5456]	235-39 [237]	79
Phenylacet aldehyde	50	Chloroform	+ve	+ve	+ve	1.536 [1.5255]	126-128 [126]	80
Monochloroacet-aldehyde	45	Chloroform	+ve	+ve	+ve	1.435 [1.403]	108-110	82

2-Chloropropion-aldehyde	45	Chloroform	+ve	+ve	-ve	1.441 [1.431]	137 Decomp.	79
Trichloroacet aldehyde [along with chloralhydrate]	50	Chloroform	+ve	+ve	+ve	1.449 [1.45572]	130-34 [131]	76
10-Undecenal-dehyde	30	Chloroform	+ve	+ve	-ve	1.416 [1.4427]	132-35	91
Olealdehyde	30	Chloroform	+ve	+ve	-ve	1.456 [1.4558]	67-70 [67-8]	91
Dimethylacr-aldehyde	45	Chloroform	+ve	+ve	+ve	1.457 [1.4528]	155-58	86
Cinnamaldehyde	50	Chloroform	+ve	+ve	+ve	1.621 [1.619]	202-205 [200-202]	90
Phenylpropiol-aldehyde	50	Chloroform	+ve	+ve	+ve	1.599 [1.6079]	188-190	79
Isobutyraldehyde	25	Chloroform	+ve	+ve	+ve	1.401 [1.372]	188-192 [187]	86
Pivalaldehyde	20	Chloroform	+ve	+ve	+ve	1.398 [1.379]	207-211 [209]	85

Note : a. Yields of aldehydes are as isolated
b. Literature values are given in parentheses.

TABLE - II

Synthesis of aldehyde from catalytic transfer hydrogenation

Acid chloride	Reaction Time (Catalyst)		Solvent	Product obtained (Aldehyde)	% yield of 2,4-Dinitrophenylhydrazone	
	ppt-Ni	ppt-Cu			ppt-Ni	ppt-Cu
Benzoyl chloride	1 hour	1.5 hours	Benzene	Benzaldehyde	73	76
Butyryl chloride	1 hour	1.5 hours	Benzene	Butyraldehyde	66	70
Isobutyryl chloride	1.5 hours	2 hours	Benzene	Isobutyraldehyde	75	77
Pivaloyl chloride	1.5 hours	2 hours	Benzene	Pivalaldehyde	77	81
Stearic acid-chloride	1 hour	2 hours	Benzene	Stearaldehyde	81	86
Oleoyl chloride	1 hours	2 hours	Benzene	Stearaldehyde	83	74
Cinnamoyl chloride	1 hours	2 hours	Benzene	Hydrocinnamal-dehyde	78	73